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Telemonitoring-based service redesign for the management of uncontrolled hypertension (HITS): Cost and cost-effectiveness analysis of a randomised controlled trial

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ABSTRACT

Objectives: To compare the costs and cost-effectiveness of managing patients with uncontrolled blood pressure (BP) using telemonitoring vs. usual care from the perspective of the National Health Service (NHS).

Design: Within trial post-hoc economic evaluation of data from a pragmatic randomised controlled trial using an intention-to-treat approach

Setting: 20 socio-economically diverse general practices in Lothian, Scotland.

Participants: 401 primary-care patients aged 29-95 with uncontrolled daytime ambulatory blood pressure (ABP) (≥135/85, but <210/135mmHg).

Intervention: Participants were centrally randomised to six months of a telemonitoring service comprising of self-monitoring of BP transmitted to a secure website for review by the attending nurse/doctor and patient, with optional automated patient decision-support by text/email (n=200), or usual care (n-201). Randomisation was undertaken with minimisation for age, sex, family practice, use of three or more hypertension drugs and self-monitoring history.

Main outcome measures: Mean difference in total NHS costs between trial arms and blinded assessment of mean cost per 1 mmHg systolic BP point reduced.

Results: Home telemonitoring of BP cost significantly more than usual care (mean difference per patient £115.32 (95% CI £83.49 to £146.63; p<0.0001)). Increased costs were due to telemonitoring service costs, patient training and additional general practitioner and nurse consultations. The mean cost of systolic BP reduction was £25.56/mmHg (95% CI £16.06 to £46.89) per patient.

Conclusions: Over the 6 month trial period, supported telemonitoring was more effective at reducing BP than usual care, but also more expensive. If clinical gains are maintained, these additional costs would be very likely to be compensated for by reductions in the cost of future cardiovascular events. Longer-term modelling of costs and outcomes is required to fully examine the cost-effectiveness implications.

Trial registration: International Standard Randomised Controlled Trials, number ISRCTN72614272.

Introduction

Hypertension is a major reversible risk factor for stroke and heart disease. It was estimated in 2001 that uncontrolled high blood pressure (BP) cost $370 billion globally (£256 billion, €413 billion) with a potential cost of $3.6 trillion (£2.5 trillion, €4.0 trillion) over a 10 year period in indirect costs.[1] Despite effective medications, BP is difficult to control for many people.[2] This is due in part to infrequent monitoring,[3] a reluctance on the part of clinicians to intensify treatment[4] and pharmacological interventions by patients.[5] Telemonitoring of BP involves patients regularly taking their own readings with onward transmission in almost real time to a website which can be accessed by themselves or by their doctor or nurse and can provide patients with decision support, in terms of when to contact a doctor or nurse for advice, which is then sent by text or email.

This paper presents a within trial, economic evaluation from the perspective of the National Health Service (NHS) of data collected during the HITS Trial.[6] This was a trial of a telemonitoring-based service redesign compared with usual care for the management of uncontrolled hypertension which was powered to detect differences in mean systolic BP but also collected resource use data as a secondary outcome. The analysis presented here, while not part of the trial protocol, was conceived prior to completion of the primary clinical analysis for the trial.

Methods

Overview of the HITS Trial

This was a six-month pragmatic, prospective, parallel-group randomised controlled trial with blinded outcome assessments. 401 patients were recruited from 20 practices representing a range of socio-economic diversity including the 5th most deprived and second most affluent in Lothian, Scotland.

Participants were included in the study if their daytime ambulatory BP averaged ≥135/85mmHg and <210/135mmHg measured by the Spacelabs 90207 Ambulatory Blood Pressure Monitor (ABPM).[7] Exclusion criteria were inability to consent, atrial fibrillation, being on the stroke or diabetes registers (as these patients would be invited to other trials in our portfolio of trials investigating the role of telemonitoring in the management of long-term conditions), treatment for cardiac event or other life-threatening illness within the past six months, major surgery within the last three months, renal failure, or hypertension not managed in primary care. A full list of baseline measurements can be found in Table 1.

Patients were randomised in a 1:1 ratio either to the telemonitoring intervention or usual care using a secure randomisation system provided by the Edinburgh Clinical Trials Unit with minimisation on the basis of age, sex, family practice, use of three or more hypertension drugs and self-monitoring history. Because simple minimisation within centres can lead to alternation of treatment allocation and potential loss of allocation concealment, a degree of random allocation was also incorporated.

Research nurses gave patients assigned to the intervention a training session on how to use the telemonitoring equipment. As the intervention comprised providing telemetric equipment, neither participants nor investigators could be masked to group assignment.

Participants were asked to monitor their own BP twice each morning and twice each evening for the first week and then at least weekly thereafter or as often as they wished. They used a validated automated sphygmomanometer (Stabil-O-Graph® mobil, IEM, Germany).[8] This linked via Bluetooth® connection to a mobile phone, which automatically transmitted readings to a central server managed by IEM Ltd (Stuttgart, Germany). Patients and clinicians could log on to a website to see the data and automated SMS texts/emails could be sent to patients informing them of the level of their control (see Box 1 for a fuller description of the process). Patients could contact clinicians if they were concerned about their BP control and clinicians could contact patients if needed to arrange modification of therapy where required. The target home-monitored BP was <135/85mmHg based on contemporaneous UK guidelines,[9] subsequently endorsed by the National Institute for Health and Clinical Excellence (NICE).[10]

Patients allocated to the usual care arm were told that the ABPM showed that their BP was uncontrolled and that they should see their GP/practice nurse for further management, but otherwise they received standard care for hypertension from their GP or nurse who were

asked to aim for a target surgery BP of <140/90mmHg based on UK guidelines (current at the time). [9]

Cost estimation

Mean costs per patient were estimated from an NHS perspective. The trial collected data by survey on the number of consultations with a general practitioner (GP), practice nurse or district nurse (separately for practice, telephone or home visits), NHS24 (emergency out-of-hours telephone helpline) contacts, out-of-office consultations with the Lothian Unscheduled Care Service (LUCS) and accident and emergency (A&E) visits. The survey was initiated at follow up by a research nurse with access to patient records. If the patient did not attend, but agreed for the data to be collected the research nurses completed the data from GP records. Data on each drug issued to each patient, the dose per day, and the number of days issued were taken from GP records from randomisation until six months after randomisation. Drugs were assumed to be the lowest cost generic treatment which matched the daily dosing structure recommended in the British National Formulary (BNF) [11] unless a specific brand was stated. Assumptions were made on an ad-hoc basis blind to treatment allocation for the 2.4% of drug entries where doses and drug combinations failed to match perfectly to the recommended dosing structure.

Unit costs were applied to each item. Where possible, these were taken from recognised national sources.[12-18] The base year for costs was the financial year 2009/10. Any estimates from different years were inflated/deflated using an appropriate inflation index (See Table 2). With the exception of equipment costs (see Table3), discounting was not required as the trial was less than one year in duration.

A detailed breakdown of the interventions costs of six months of BP telemonitoring, assumptions made in their estimation, price weights applied, inflation indices used and their sources is given in Table 3. The price of the full six months of intervention was applied uniformly to all patients in the monitored group, regardless of whether or not they completed the trial.

Although data were collected on the number of hospital admissions attended by each patient during the trial, the cost of hospital admissions can vary substantially depending on the nature of the admission[15,19] and specific details of the nature of each admission were not

recorded in the survey. Instead, reported admissions were matched with entries in the adverse events log for the trial to generate verbal descriptions of each event. BM viewed the extracted descriptions of each event blind to randomisation allocation, assigned Healthcare Resource Group (HRG4) codes based on the descriptions and assessed whether the event could be at least be possibly related to BP management. HRG4 codes are used in the NHS to group procedures into categories of hospital care which incur similar resource use.

Of the 28 admissions recorded in the adverse events log seven (25%) were for cardiovascular related diagnoses and as such were deemed indirectly related to high blood pressure or related to dizziness or falls for which blood pressure could not be ruled out as a contributing factor. None could specifically be related to telemonitoring itself. The decision therefore was made not to include these costs in the base case analysis as there was a risk of overwhelming the more robust estimates of other cost factors with unreliable, and likely unrelated, admission costs. However, a sensitivity analysis was undertaken including the costs of hospital admissions where price weights were applied from the Scottish National Tariff[19] based on the HRG4 code selected.

Effect variable

The effect variable for the cost-effectiveness analysis was mean daytime systolic ambulatory blood pressure (SABP). We therefore calculated cost per mmHg systolic BP reduced over the six months intervention period.

Analysis

All analyses were undertaken on an intention-to-treat basis.

Missing data

Primary outcome data were missing for 11.5% of patients including 20 participants (six in the intervention group and 14 in the usual care group) were either lost to follow-up or who withdrew consent. Economic variables were missing for 0 to 8.7%. In total 21.9% of patients had missing data for at least one variable of interest. Multiple imputation by chained equations[20] was used to create 10 imputed datasets by imputing incomplete variables under

fully conditional specification. This was based on age, sex, body mass index (BMI), BP (systolic and diastolic), number of hypertension drugs, cholesterol, exhaled per cent carbon monoxide, blood HbA1c, Euroqol-5D(EQ-5D) responses and all healthcare resource use variables. Calculations were undertaken in STATA 12 using the "mi ice" command. Normally distributed parameters (including primary outcome data) were imputed using multiple regression by ordinary least squares; ordered categorical variables were imputed using ordinal logistic regression and other non-normal variables imputed using predictive mean matching. Model parameters were then estimated using the respective regressions techniques described below. These estimates and their standard errors were combined using Rubin's rules.[21]

Cost analysis

Univariate analysis was undertaken of differences between trial arms in terms of total costs and each cost sub-element. As the cost data were non-normally distributed with a heavy right skew and long tail, testing was performed using non-parametric bootstrap of differences in mean patient costs between trial arms and bias corrected confidence intervals and p-values (two tailed) were reported for each cost item with significance set at the 5% level.

Cost-effectiveness analysis

Baseline resource use was not recorded. We would expect randomisation to balance out baseline costs between groups. However to counteract any baseline imbalances, point estimates for incremental costs were estimated using a generalised linear model (GLM) controlling for age, sex, baseline systolic BP and baseline health related quality of life (calculated by baseline EQ-5D index score[22]). GLMs allow adjustments to be made for heteroscedasticity and skew by the adoption of a 'family' and link function.[23,24]

Family function was selected by Modified-Parks test[24] and a power function for the link was selected on the balance of p-values from three tests of fit as recommended by Glick et al.[23] These tests were, the Modified Hosmer & Lemeshow test (tests for systematic bias in fit on raw scale), the Pregibon link test (tests for linearity of response on scale of estimation), and Pearson correlation test (tests for systematic bias in fit on raw scale). The Gaussian family was selected and a power of 0.5343 was selected for the link function.

For incremental BP point reduction, multiple regression (by ordinary least squares) was used controlling for all minimisation variables namely: age; sex; general practice; use of three or more hypertension drugs and self-monitoring history. This was selected for its equivalence to the analysis used for the variable in the primary analysis.[6]

Incremental cost-effectiveness ratios (ICERs) were expressed as cost per 1 mmHg systolic BP point reduced. Bias-corrected confidence intervals[22] for the ICERs were estimated from the bootstrapped data generated using the "recycled predictions" method as described by Glick et al.[23] This technique generates a large number of bootstrapped samples (10,000 replications were used). The chosen regressions for each variable were used to estimate incremental costs, BP and their respective ICERS within each sample.

The proportion of samples in which the intervention is shown to be cost-effective to the NHS at a given price per mean systolic mmHg (using the net benefit technique[26]) is used to estimate the probability that the intervention is cost-effective at that price. The process was repeated varying the price over a range between £0 and £100 per systolic mmHg to plot cost-effectiveness acceptability curves (CEACs).CEACs show the probability the treatment is cost-effective at varying costs (willingness on behalf of the NHS to pay) per unit of outcome (1 mmHg systolic BP reduced) to a decision maker.

As several assumptions were made in the intervention costs (see Table 3), as a sensitivity analysis, CEACs were calculated with the total cost of six months of intervention varied in increments of 25% to +/- 100% of the base case price (See Figure 3).

Results

Analysis of costs

Table 4 details the results of the univariate analysis of costs and resource use per patient associated with each trial arm. The mean total estimated healthcare cost per patient was £287.18 in the intervention group and £177.95 the usual care group (mean difference £109.23, 95% CI £76.36 to £140.63) in univariate analysis. Controlling for baseline characteristics in the multivariate analysis gave similar results with a mean total costs of £290.13 in the intervention group and £174.81 in the usual care group (mean difference £115.32, 95% CI £83.49 to £146.63).

The difference in total costs remained significant with the cost of the telemonitoring technology excluded from the analysis demonstrating that NHS costs rose outside of the cost of the intervention itself. This was driven largely by a significant increase in mean costs arising from approximately one additional GP surgery consultation and half a practice nurse surgery consultation per person in the intervention group compared with the usual care group. The only other significant cost element difference was approximately half an additional practice nurse phone consultation. No other cost element was significantly different between the groups. This included the cost of prescribed medication. Despite a significantly greater increase in the doses of prescribed medication in the telemonitored group over that of the usual care group,[6] the rise in cost was relatively trivial as often higher strength medications were priced similarly to lower strengths.

In sensitivity analysis, the mean cost of hospital admissions in the intervention arm were £287.01 compared with £181.54 in the control arm (mean difference £105.47, 95% CI £-123.16 to £402.40; p=0.4242) which raises the mean difference in total NHS costs to £214.70 (95% CI £-23.71 to £526.65; p=0.0982). However, this estimate was dominated by one patient in the intervention arm with repeated admissions for the treatment of an infected wound and related scare tissue costing over £17,000, none of which were assessed to be possibly related to blood pressure management. When the costs of these admissions of this patient were excluded, the equivalent mean differences in hospital costs fell to £16.56 (95% CI £-188.04 to £202.17; p=0.8456) and total costs to £125.79 (95% CI £-88.85 to £318.40; p=0.2232).

Analysis of blood pressure point reduction

Following imputation, the mean daytime SABP fell in both groups, from 146.20mmHg to 140.15mmHg in the telemonitoring arm and 146.22mmHg to 144.50mmHg in the usual care arm. The difference in mean daytime SABP at six months between the two arms (i.e. control-telemonitoring) was 4.51 mmHg (95%CI 2.49 to 6.61; p<0.0001), adjusted for baseline mean daytime SABP and minimisation factors.

Cost-effectiveness analysis

Figure 2 shows the joint distribution of incremental costs and incremental systolic blood pressure point reduction generated by the bootstrap replicates. In all replicates, costs per patient were higher and mean SABP per patient was lower in the monitored group than the control (p<0.0001 for both variables). This indicates that the telemonitoring was both more

costly and more effective than usual care in all replicates. The ICER was £25.60/mmHg (95% CI £16.05 to £46.69).

Figure 3 shows the probability of telemonitoring being cost-effective at varied NHS willingness to pay per BP point reduction. The 100% line represents the base case analysis with intervention costs at £70.77 and the other lines showing how the CEAC would change if intervention costs were higher or lower.

Discussion

Over the six months of the trial, the intervention was significantly more effective than usual care, but also significantly more costly, on average lowering SABP by 4.51mmHg and raising total cost by £115.32. The increase in costs was predominantly driven by the estimated intervention costs (£70.77) and increased costs associated with telemonitored patients using on average approximately one additional GP surgery consultation and half a practice nurse surgery consultation. Although telephone consultations with the practice nurse and their costs also significantly rose (by approximately half a call on average), the costs for these were relatively small and had little impact on total cost.

The trial found a significant increase in the dosages of medication issued[6] which may explain some of the additional consultations as they were likely to have been required for prescribing and monitoring of patients during transition to a new drug/dose. Interestingly however medication costs did not rise significantly in spite of this intensification. This is due to higher dosage pills often costing less per dose than lower dosage pills when costs of generic treatments are used for these estimates.[16] There is a risk that the way in which the medication costs were estimated (selecting a generic where available and selecting the lowest cost option that matched dosing recommendations[11]) could have contributed substantially to this finding. However, such an approach does at least attempt to estimate the difference in costs attainable under best practice assuming this includes the selection of the lowest cost drug based on active agent.

It should be noted that our accompanying qualitative study[27] suggests that over the trial, clinicians found face-to-face communication with patients was not necessary to support BP telemonitoring and that they substituted some of these forms of consultation with other modes of communication: mainly telephone and on two occasions email. Both patients and clinicians thought that in the longer-term BP telemonitoring would reduce the need for

surgery visits. Thus a reduction in the GP consultations element of the overall costs may be realised in the longer-term. This has been found in previous studies of telemonitoring where consultation costs were lower.[28,29,30]

The remaining cost elements were also non-significantly different between groups and played relatively minor roles in the overall total cost differences.

In sensitivity analysis, hospital costs were non-significantly higher on average in the intervention group than in the control by £105.47 raising differences in mean total costs to £214.70. However differences in costs of hospital admissions were exaggerated by the inclusion of an outlier patient in the intervention arm unrelated to blood pressure management. With these excluded, hospital costs were similar in both arms with an insignificant difference of £16.56. In both cases uncertainty surrounding hospital cost dominated uncertainty surrounding total cost figures. Hence when hospital admissions are included in total costs estimates we are no longer confident that the cost of resource use outside of the intervention service itself was higher or lower in the intervention group because secondary care costs have the potential for the largest financial impact on the NHS. However there are strong reasons to doubt that any of the hospital admissions observed during the trial were related to the patient's current BP, even those of a cardiovascular nature. This is because it is possible that events resulting in hospital admission may well have been set in motion prior to the onset of the study though we lack data to confirm this either way. A recent meta-analysis also found no link between home blood pressure telemonitoring and short term rates of adverse events.[28]

Dividing per patient mean differences in costs by per patient mean differences in blood-pressure reduction yields an ICER of £25.56/mmHg. Whilst on the face of it modest, there are to our knowledge no criteria available to assess the cost-effectiveness of the value of a BP point reduction, hence no formal assessment of whether this constitutes evidence that the intervention is cost-effective or not can be offered. It should also be recognised that £25.56/mmHg is a ratio rather than a tariff. It is perhaps more accurate to say that over the first 6 months of the intervention we estimate that BP will reduce on average by 4.51 mmHg at a cost of around £115.32 per patient.

It is not known if the improved BP control found in the trial would be sustained once telemonitoring ceased. However, If sustained over 10 years, this type of reduction would be expected to lead to a >15% reduction in risk of stroke and >10% reduction in risk of coronary

heart disease.[29] The costs incurred in the intervention period were low relative to the several thousand pounds likely to be spent on a cardiovascular event.[15,19,32] For example, Youman et al[32] calculated the cost of a stroke to the NHS in 2001 to be £15,306 over five years. Should the blood-pressure point reduction be sustained beyond the observed six months examined here, the expected reduction in cardiovascular events[31] may mean that that the intervention is dominant over usual care in the long term, that is to say both more effective and cost saving. Estimating this would require a study with a much longer follow-up or, perhaps more realistically, mathematical modelling of longer-term health costs and benefits. Longer term follow up of the participants is planned to determine the extent to which the difference in systolic BP persists after the end of the trial, which will be vital data to underpin such modelling.

Strengths and limitations

Unlike many previous studies, we used ABPM to measure BP. This is a considerable strength as ABPM is considered the gold standard for BP measurement and lends greater generalisability to the results as it is now recommended practice in the UK to diagnose high BP with ABPM.[10] The generalisability is further strengthened by the pragmatic setting, intention to treat analysis, the broad socioeconomic profile of participants and the absence of restrictions on participant age (oldest patient was 95) or exclusion on the basis of maximal treatment. The results may be less generalisable outside of a UK context as this is beyond the scope of this analysis.

The analysis was not part of the original trial protocol. It was however conceived prior to commencing the primary clinical analysis the usual limitations of post hoc analysis are less relevant. This did however mean that the cost analysis was restricted by the variables available in the dataset and that some cost elements have not have been accounted for, most notably outpatient visits. On the other hand, the variables that were collected were similar to those used in other trials and are likely to be robust as surveys were completed with access to medical records.

It was not possible to control for baseline cost in multivariate analysis as these were not recorded. Instead, the analysis relies on baseline SABP and health related quality of life and on the randomisation process in its place. While it is possible that a different result may have been observed should baseline costs have been available for use, we do not anticipate that

this would have differed considerably from the results presented here as it is not unreasonable to expect both of these factors to be highly correlated with baseline costs. Selection bias is very unlikely to have occurred during the randomisation/minimisation process as this service was provided remotely by clinical trials unit.

Randomisation was at the level of the participant. Although this raises the possibility of clustering effects, the numbers of study participants within each practice constituted a tiny proportion of all such patients and the risk of significant contamination is therefore small. A post-hoc cluster analysis revealed a low intra-cluster correlation coefficient and did not alter the outcome, suggesting that clustering did not have a major effect. In this situation, a cluster-randomised trial may have been more open to bias than a participant-level randomised trial.[33]

It was not possible to determine if £25.56 per mmHg reduced would be considered cost-effective or not. Using the NICE criteria for cost-effectiveness, the value of interventions are interpreted in terms of long term cost per quality adjusted life year (QALY) gained.[34,35] The EuroQol EQ-5D survey from which QALYs can be calculated[22] was included in the trial.[6] However, without sufficient power or follow-up to detect major cardiovascular events, differences in quality of life observed in the trial period would be unlikely to manifest themselves in an asymptomatic condition. Moreover, given that the participants were not blind to the intervention this might be open to bias. Hence QALYs could not reliably be estimated in this context. They are arguably better left to be determined by longer term modelling.

Comparisons to similar studies

Caution is advised when comparing studies of telemonitoring as the services within which the telemonitoring is nested often vary substantially and it is the combined effect of the telemonitoring and other interrelated services which are observed.

Two recent systematic reviews of BP telemonitoring, found few studies which included measures of healthcare utilisation and/or cost. Of those which did, office visits are frequently the only health care resource considered outside of the direct cost of the technology issued[28,36] and none were based in a UK setting, though a UK study by McManus et al suggests that an accompanying cost-effectiveness analysis is forthcoming.[29]

Meta-analyses of home BP telemonitoring versus usual care by Omboni et al 2012 find home BP telemonitoring to be associated with increased medication use, reduced office visits and increased overall healthcare costs, though medication use and overall healthcare casts suffered from heterogeneity between studies.[28] While the increased prescribing is in line with our own findings, the decreased office visits are not. As a result Omboni et al attribute the rise in healthcare costs to the cost savings in terms of office visits being more than offset by equipment costs where our findings suggest an increase in both.[28]

An explanation for this disparity may come from the heterogeneity of the services being delivered alongside the telemonitoring. For example, McManus et al. showed that adding a medication self-titration plan to BP telemonitoring produced similar reductions in BP to our study, but found no increase in face to face consultations with physicians.[29] This lends strength to the possibility that many of the increased GP surgery visits observed in this trial were required for prescribing.

Comparisons of healthcare costs with studies outside of the UK can also be problematic as different social insurance systems jeopardise cross-border generalisability, indeed Omboni et al attribute the heterogeneity in their analysis of healthcare costs to this issue.[28]

Madsen et al compared the cost-effectiveness of a similar intervention with usual care from a Danish health service perspective.[30] In contrast to our findings, they found higher consultation and medication costs in their control arm. Again these were more than offset by equipment costs leaving total costs significantly higher in the intervention arm however SABP was non-significantly higher in the intervention arm by 2.8mmHg. The authors attribute the raised medication costs to significantly increased prescribing of AT2-antagonists in the control arm. This intensification in prescribing in the usual care group rather than the intervention group as in our trial may go some way to explaining the lower reduction in blood pressure observed. However the fact that point estimates were still in favour of the intervention suggests that medication prescribing may not be the only factor influencing BP.

Conclusions

In conclusion, although more expensive to the NHS than usual care, telemonitoring of BP in primary care was more effective at reducing blood pressure during the 6 months of

intervention. These costs may be recuperated in the long term as a result of prevention of future cardiovascular events if the reduction in BP is maintained. Further research is required to determine if the BP improvement is sustained and, if so, what impact this has on cost-effectiveness.

Footnotes

Contributors**:** Brian McKinstry, Janet Hanley, Sarah Wild, Claudia Pagliari and Paul Padfield designed the trial. Janet Hanley and Brian McKinstry led lead the research. Mary Paterson was trial manager, Steff Lewis planned and supervised the statistical analysis, Ashma Krishan carried out the statistical analysis, Andrew Stoddart carried out the economic analysis and wrote the first and subsequent drafts of the paper, Aziz Sheikh provided advice throughout the trial. All authors critically revised the drafts and have approved the submission of the final paper.

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Competing interests: All authors have completed the Unified Competing Interest form atwww.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work

Ethical approval: The study was approved by Lothian Research Ethics Committee REC reference number: 08/S1101/38. Written informed consent was obtained from all participants**.**

Data sharing: Anonymised datasets may be available from the corresponding author on application.

Box 1: Description of the telemonitoring intervention (See web supplemental files for illustrations)

The intervention:

The practices and participants were asked to use a system which comprised a validated electronic home BP monitor and mobile phone technology that enabled the transfer of BP readings via SMS to a secure website which was accessible to the user and their doctor or nurse, and also provided automated feedback to the patient. The BP monitor linked to a mobile phone wirelessly, via Bluetooth. The components of the intervention were:

Home BP monitoring: Participants were asked to record their BP as agreed with the healthcare team, or more frequently as they wished. Guidance was initially to record BP twice in the morning and twice in the evening for a week in line with the European guideline on BP monitoring,[37] to build a baseline average. Thereafter, they were asked to take weekly measurements preferably at different times of day if their average BP was within the recommended range, but if they had made any lifestyle or medication change which would impact on their BP, they were asked to measure their BP for a more intensive period of monitoring to allow the rolling average to change and to more quickly assess the effect.

Transmission of data: This simply required the phone to be switched on and to have a signal when the BP measurement was taken. Participants just had to apply the cuff and press a button on the BP monitor. The reading and transmission occurred automatically. Mobile phone problems did not lead to loss of data because all readings were stored in the monitor and any un-transmitted readings were sent when the next reading was taken.

Feedback to patient participants (closed loop feedback): In addition to optionally accessing their BP record on-line, participants could also opt to receive reports via text message or email. These gave advice on the current status of their BP based on the average of the last 10 readings, and whether they should contact their doctor or nurse. Reports were generated every 10 readings or weekly, whichever was sooner, with a reminder to check BP if this had not been done. These reports could reassure them that their average BP was within target (<135/85mmHg)or tell them that their BP average was improved on the last report but not yet to target and to maintain current therapy, or that their BP was not at target and that they should contact their clinician. If an individual BP reading was very high (>220/120mmHg) an immediate text or email report was generated reinforcing the written advice in the patient information leaflet to rest for 30 minutes, check again and contact the practice if BP remained very high.

Sharing the readings with the healthcare team: Members of the healthcare team were able to access the records of their patients online via a secure login to a summary screen which listed their patients, their average BP over the last 10 readings, and the date of their last reading. Average BPs outside the recommended limits (set at 135/85mmHg for the study) were highlighted. Clicking on the each individual patient led to lists or graphs of all their readings. Clinicians could then check their patients' electronic GP record to see if there had been recent advice regarding medication or lifestyle change and if not, could contact the patient to make a change. Clinicians were recommended to check the website weekly, but the frequency of log-on could be chosen by them.

Usual Care

Participants allocated to the usual care group were asked to continue to attend the practice for BP checks according to the usual routine of the practice. If they were already home monitoring they were not discouraged from continuing.

All participants

For all participants the GP/practice nurse were informed that the ambulatory monitoring used to screen for eligibility for the HITS trial had shown that their average BP was above the target range, but they were not given the actual reading. All participants were given an information pack containing a range of publicly available leaflets on hypertension management and lifestyle modification.

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Table1. Baseline characteristics for full dataset

Variable		Monitored (N=200)	Control (N=201)
Age (Years) Mean (SD)		60.5 (11.8)	60.8 (10.7)
Male N (%)		117 (58.5)	120 (59.7)
Blood pressure self-monitoring history N (%)			
Never		128 (64.0)	126 (62.7)
Occasionally		56 (28.0)	56 (27.9)
Regularly		16 (8.0)	19 (9.5)
Body-mass index (kg/m^2) Mean (SD)		30.1 (5.7)	30.2 (6.2)
Smoking N (%)			
Yes		23 (11.5)	20 (10.0)
Mean (SD) (cigarettes/day)		17.6 (9.2)	14.9 (10.4)
No		177 (88.5)	181 (90.0)
Alcohol use[i] N (%)			
Yes		158 (79.0)	159 (79.1)
Median (1st, 3rd Quartile)[units of alcohol(10mls)/day]		1.7 (0.9, 2.9)	2.0 (0.7, 4.0)
No		37 (18.5)	41 (20.4)
Exhaled Carbon Monoxide category N (%)			
Non-smoker (1-6)		177 (88.5)	179 (89.1)
Light smoker (7-10)		0 (0.0)	3 (1.5)
Moderate smoker (11-20)		8 (4.0)	11 (5.5)
Heavy smoker (20+)		15 (7.5)	8 (4.0)
Cholesterol level (mmol/L)[ii] Mean (SD)		5.5 (1.0)	5.3 (1.0)
HbA1c level (%)[iii] Mean (SD)		37.7 (6.5)	37.7 (5.4)
Urinary Sodium/CreatinineRatio[iv] Mean (SD)		9.7 (5.4)	10.9 (8.7)
Surgery measured Systolic BP (mmHg) Mean (SD)		152.9 (15.1)	152.4 (14.3)
Surgery measured Diastolic BP (mmHg) Mean (SD)		92.1 (11.5)	89.9 (11.3)
Daytime Ambulatory Systolic BP (mmHg) Mean (SD)		146.2 (10.6)	146.2 (10.5)
Daytime Ambulatory Diastolic BP (mmHg) Mean (SD)		87.1 (10.0)	85.4 (9.6)
HADS[29] Anxiety Score[v] Mean (SD)		5.0 (2.9)	5.1 (3.6)
HADS Depression Score[v] Mean (SD)		2.8 (2.4)	2.9 (2.5)
Exercise Tolerance Score[35vi] Mean (SD)		7.8 (2.9)	7.6 (3.0)
Stanford Self Efficacy Questionnaire (short version)[36vii] Mean (SD)		8.7 (1.4)	8.5 (1.4)
Morisky Medication Adherence Scale[37] N (%)			
Sometimes forgets to take medication[viii]:	Yes	61 (30.5)	63 (31.3)
	No	132 (66.0)	132 (65.7)
Sometimes careless about taking medication[ix]:	Yes	24 (12.0)	23 (11.4)
	No	169 (84.5)	173 (86.1)
Sometimes stops taking medication when feels better[x]:	Yes	11 (5.5)	15 (7.5)
	No	181 (90.5)	180 (89.6)
Sometimes stops taking medication when feels worse[xi]:	Yes	18 (9.0)	22 (10.9)
	No	170 (85.0)	173 (86.1)
Number of defined daily doses of hypertension drugs Median (1st, 3rd Quartile)		1.5 (1, 3)	1.7 (1, 3)
EuroQol-5D[23xii] Mean (SD)		0.875 (0.177)	0.857(0.220)

Missing data-[i]5 in Monitored & 1 in Control group.[ii]5 in Monitored & 8 in Control group. [iii]7 in Monitored & 9 in Control group. [iv]4 in Monitored & 2 in Control group. [v]2 missing in each group. [vi]1 in Monitored & 2 in Control group. [vii]6 in Monitored & 1 in Control group. [viii]6 in Monitored & 7 in Control group. [ix]5 in Monitored & 7 in Control. [x]6 in Monitored & 8 in Control. [xi]6 in Monitored & 12 in Control group. [xii] 5 in Monitored and 6 in Control group

Table2. Price weights, calculations and sources

Variable	Value		Unit	Source(s) / Notes
General Practitioner:				
Surgery	£36.00	per	consultation	[12]
Home	£120.00	per	consultation	[12]
Phone	£22.00	per	consultation	[12]
Practice Nurse:				
Surgery	£12.00	per	consultation	[12]
Home	£20.00	per	consultation	[12]
Phone	£4.74	per	consultation	Cost per hour[12] x Average Call length[13]
District Nurse:				
Surgery	£18.86	per	consultation	Cost per hour[12] x Average consultation length.[13] Consultation length assumed to be equal to that of a practice nurse.
Home	£27.00	per	consultation	[12]
Phone	£10.46	per	consultation	Cost per hour[12] x Average Call length. [13] Call length assumed to be equal to that of a practice nurse.
NHS 24 Contact	£41.71	per	contact	£35.69[14] inflated to 2009/10 prices using Hospital & Community Health Services (HCHS) pay and price inflation index[12])
LUCS Consultation	£64.82	per	consultation	Number of LUCS contacts divided by total budget, obtained private communication with NHS Lothian. Information on cost per consultation was not available.
A&E Visit	£95.00	per	visit	[15]
Medication	All medication use recorded was priced individually using the 2011 prices from the MIMS data base[16] deflated to 2009 prices using the Pharmaceutical Inflation component of the CPI[38] with adjustments made for 10.5% claw back[17] and container costs.[18]			
HBPM Service & Device	£70.77	for	6 months	Per patient. See Table3

Table 3. Price estimation and components for cost of intervention over 6 months (per patient)

Variable	Value		Unit	Source(s) / Notes
Home Blood Pressure Monitor (HBPM):				
Initial Training of Patient in Device Use	£12.00	per	patient	One off patient training in use of device. Priced as an assumed 20 minutes of practice nurse time (£36 per hour client contact[12]) based on the trial's pilot work
HBPM Device	£53.11 £1.20	per	each month*	Local pricing from manufacturer invoice (60 Euro converted to GBP using average exchange rate 2009/10[39]).
Mobile Phone	£48.48 £1.44	per	Each month*	Local pricing from internal communications with NHS Lothian telecoms (£49)) deflated from 2011 prices to 2009/10 using medical products component of CPI. [38]
Server Hosting	£0.42	per	month	Local pricing from Supplier Invoice (£1000 per year for all patients, divided by 200 patients over 12 months)
Web Hosting	£2.59	per	month	Local pricing from Supplier Invoice (3.10 Euro converted to GBP using average exchange rate 2009/10[39])
Sim Card	£1.98	per	month	Local pricing from internal communications with NHS Lothian telecoms (£2 deflated from 2011 prices to 2009/10 using medical products component of CPI[38]).
Nurse Time	£2.17	per	month	Assumption of 1 min per week of practice Nurse time spent checking incoming HBPM data (£30 per hour non-specific work[12]) based on anecdotal information.
Total**	**£70.77**	**for**	**6 months**	

* *Per month costs of HBPM Device and Mobile phone calculated using the annuity method[40] at a discount rate of 3.5% per year as recommended by NICE.[34] Assumed lifespan of device: 4 years, assumed life of mobile phone: 3 years.*

** *Total does not match sum of components due to rounding of values.*

Table4. Estimated Mean (Standard Error) Healthcare Service Resources Used And Associated Costs Per Patient By Factor

	Monitored Group (N=200)				Control Group (n=201)				Mean Difference (95% Confidence Interval*)		P-value*
	No. Used		*Cost, £*		*No. Used*		*Cost, £*				
GP Consultations:											
Surgery Consultations	*3.61*	*(0.19)*	*130.00*	*(7.00)*	*2.70*	*(0.21)*	*97.11*	*(7.46)*	*32.89*	*(14.55 to 51.04)*	*0.0006*
Phone Consultations	*0.57*	*(0.08)*	*12.43*	*(1.78)*	*0.49*	*(0.09)*	*10.69*	*(1.98)*	*1.74*	*(-2.74 to 6.09)*	*0.4466*
Home Consultations	*0.06*	*(0.03)*	*7.74*	*(3.24)*	*0.09*	*(0.04)*	*10.39*	*(4.52)*	*-2.65*	*(-11.91 to 5.27)*	*0.5528*
Total Consultations	4.24	(0.23)	150.17	(8.90)	3.27	(0.27)	118.19	(10.52)	31.97	(8.38 to 54.22)	0.0044
Practice Nurse Consultations:											
Surgery Consultations	*1.90*	*(0.18)*	*22.75*	*(2.11)*	*1.41*	*(0.14)*	*16.88*	*(1.71)*	*5.86*	*(1.14 to 11.00)*	*0.0156*
Phone Consultations	*0.69*	*(0.09)*	*3.28*	*(0.42)*	*0.15*	*(0.05)*	*0.71*	*(0.25)*	*2.57*	*(1.75 to 3.45)*	*<0.0001*
Home Consultations	*0.02*	*(0.01)*	*0.41*	*(0.28)*	*0.01*	*(0.01)*	*0.30*	*(0.27)*	*0.11*	*(-0.38 to 0.77)*	*0.7042*
Total Consultations	2.61	(0.21)	26.43	(2.27)	1.57	(0.17)	17.89	(1.88)	8.54	(3.46 to 14.15)	0.0016
District Nurse Consultations	0.04	(0.02)	0.67	(0.41)	0.15	(0.11)	3.94	(3.05)	-3.26	(-11.94 to 0.39)	0.2486
NHS24 Consultations	0.10	(0.03)	4.03	(1.39)	0.05	(0.02)	2.12	(0.79)	1.91	(-0.42 to 4.95)	0.1386
LUCS Consultations	0.07	(0.02)	4.34	(1.39)	0.04	(0.02)	2.48	(1.16)	1.86	(-0.89 to 4.83)	0.1930
Medication			24.07	(2.12)			23.59	(2.20)	0.48	(-5.83 to 6.40)	0.8682
Accident and Emergency Visits	0.07	(0.02)	6.70	(2.24)	0.10	(0.03)	9.74	(2.98)	-3.04	(-8.87 to 2.47)	0.2856
Subtotal Excluding Tele-monitoring			**216.41**	**(11.66)**			**177.95**	**(15.15)**	**38.46**	**(5.59 to 69.87)**	**0.0194**
Tele-Monitoring Service & Device			70.77						70.77		
Total Healthcare Costs			**287.18**	**(11.66)**			**177.95**	**(15.15)**	**109.23**	**(76.36 to 140.63)**	**<0.0001**

* : P-values (two-tailed) for significant difference from zero and Bias corrected confidence interval estimated by non-parametric bootstrap (10,000 replications)

LUCS : Lothian Unscheduled Care Service (out of hours GP or nurse consultations)

Figure 1. Consort Diagram

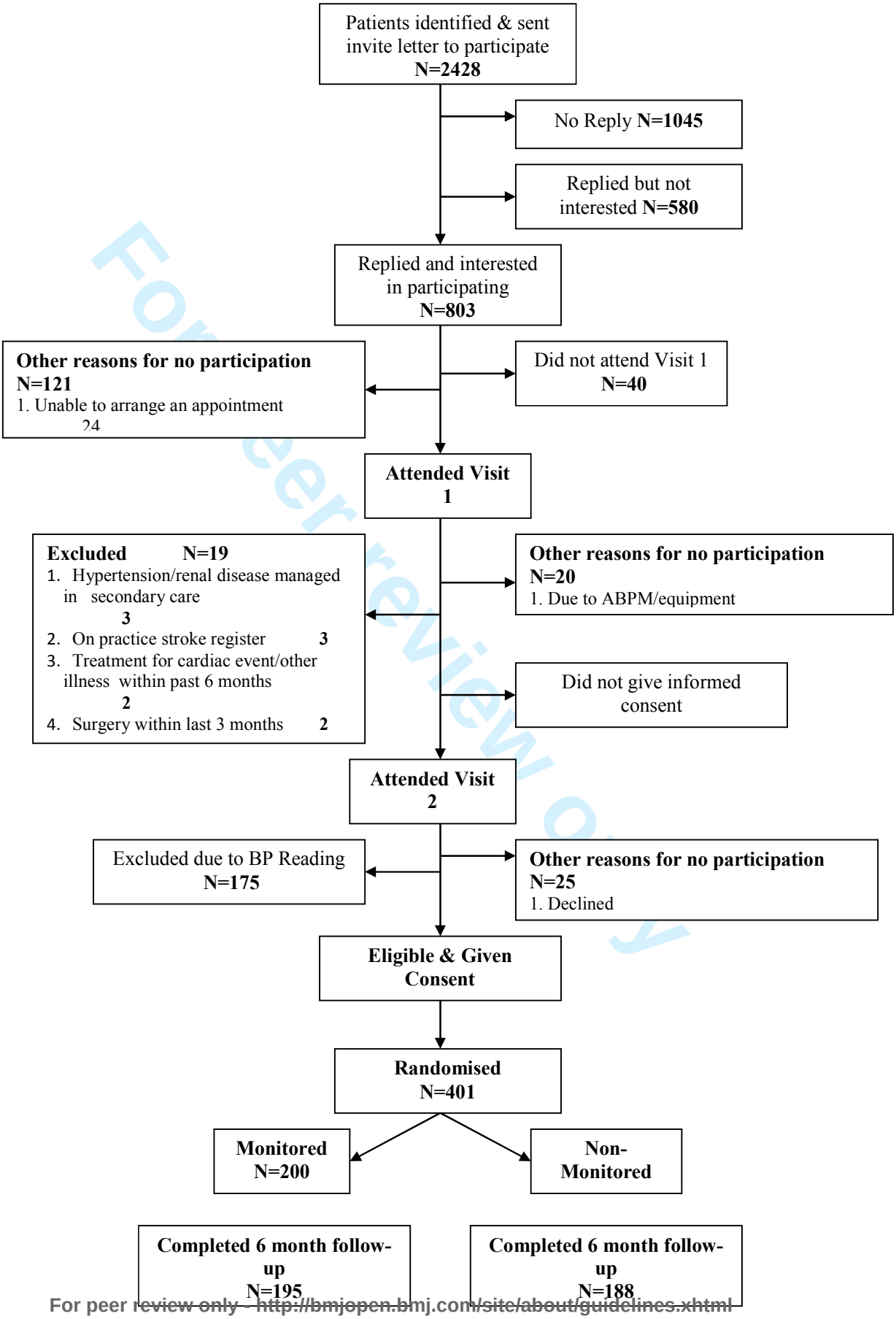


Figure 2.

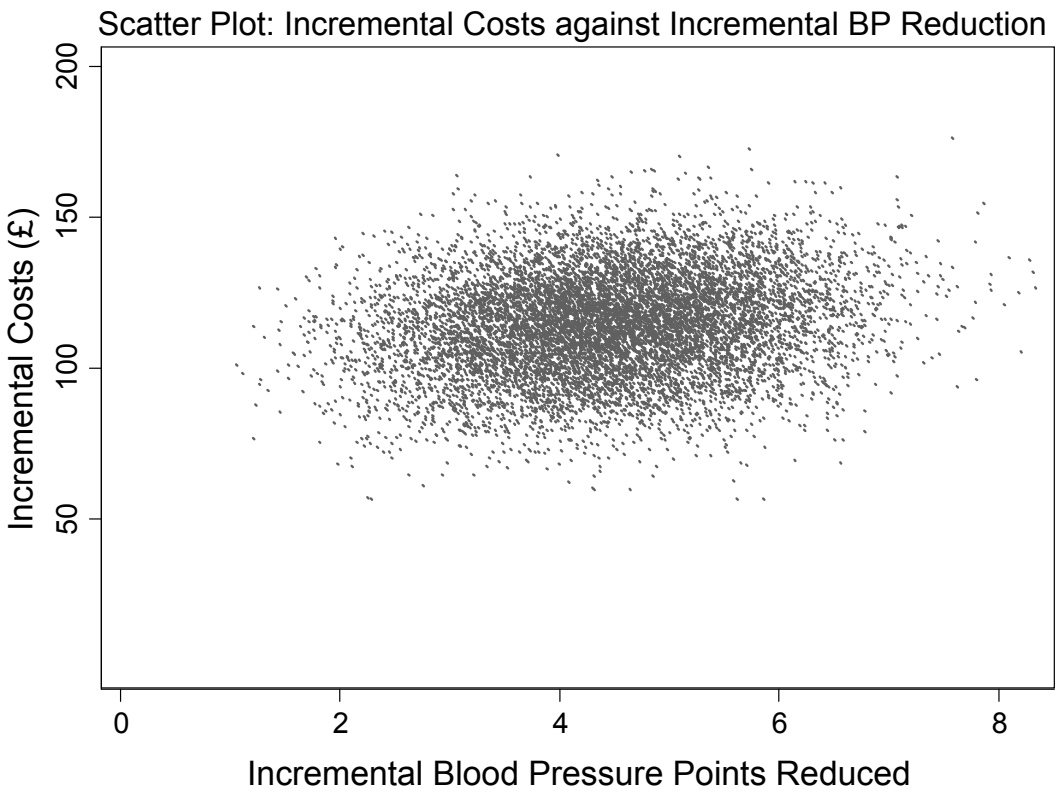
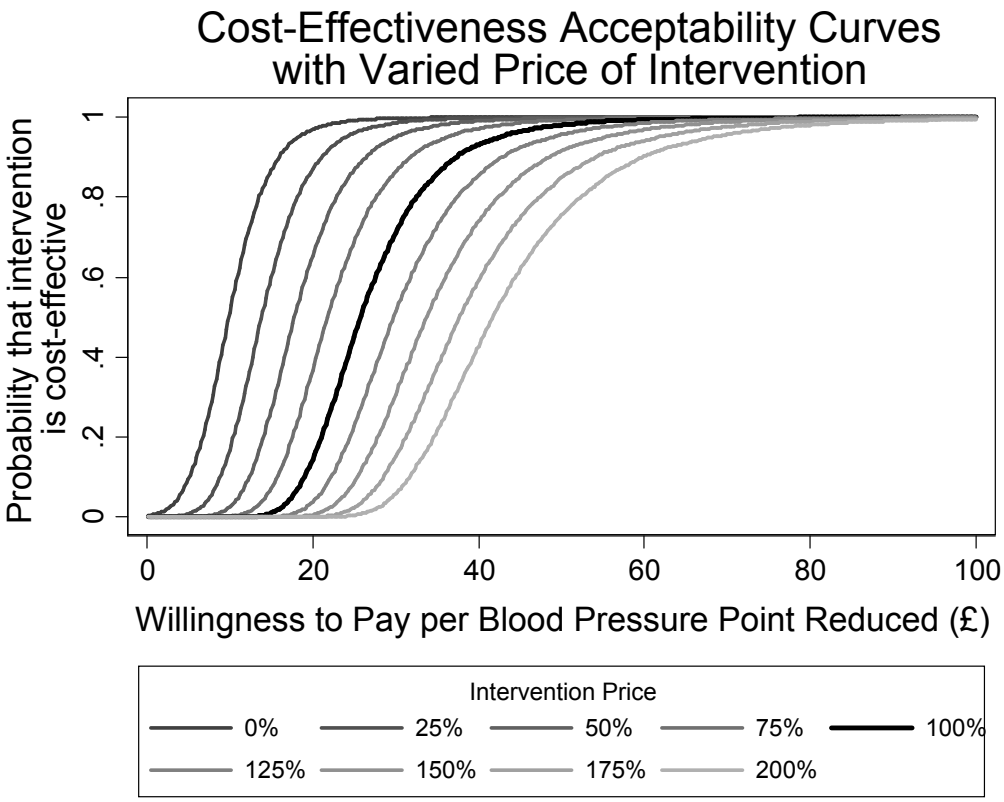


Figure 3.



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ABSTRACT

Objectives: To compare the costs and cost-effectiveness of managing patients with uncontrolled blood pressure (BP) using telemonitoring vs. usual care from the perspective of the National Health Service (NHS).

Design: Within trial post-hoc economic evaluation of data from a pragmatic randomised controlled trial using an intention-to-treat approach

Setting: 20 socio-economically diverse general practices in Lothian, Scotland.

Participants: 401 primary-care patients aged 29-95 with uncontrolled daytime ambulatory blood pressure (ABP) (≥135/85, but <210/135mmHg).

Intervention: Participants were centrally randomised to six months of a telemonitoring service comprising of self-monitoring of BP transmitted to a secure website for review by the attending nurse/doctor and patient, with optional automated patient decision-support by text/email (n=200), or usual care (n-201). Randomisation was undertaken with minimisation for age, sex, family practice, use of three or more hypertension drugs and self-monitoring history.

Main outcome measures: Mean difference in total NHS costs between trial arms and blinded assessment of mean cost per 1 mmHg systolic BP point reduced.

Results: Home telemonitoring of BP cost significantly more than usual care (mean difference per patient £115.32 (95% CI £83.49 to £146.63; p<0.001)). Increased costs were due to telemonitoring service costs, patient training and additional general practitioner and nurse consultations. The mean cost of systolic BP reduction was £25.56/mmHg (95% CI £16.06 to £46.89) per patient.

Conclusions: Over the 6 month trial period, supported telemonitoring was more effective at reducing BP than usual care, but also more expensive. If clinical gains are maintained, these additional costs would be very likely to be compensated for by reductions in the cost of future cardiovascular events. Longer-term modelling of costs and outcomes is required to fully examine the cost-effectiveness implications.

Trial registration: International Standard Randomised Controlled Trials, number ISRCTN72614272.

Introduction

Hypertension is a major reversible risk factor for stroke and heart disease. It was estimated in 2001 that uncontrolled high blood pressure (BP) cost $370 billion globally (£256 billion, €413 billion) with a potential cost of $3.6 trillion (£2.5 trillion, €4.0 trillion) over a 10 year period in indirect costs.[1] Despite effective medications, BP is difficult to control for many people.[2] This is due in part to infrequent monitoring,[3] a reluctance on the part of clinicians to intensify treatment[4] and pharmacological interventions by patients.[5] Telemonitoring of BP involves patients regularly taking their own readings with onward transmission in almost real time to a website which can be accessed by themselves or by their doctor or nurse and can provide patients with decision support, in terms of when to contact a doctor or nurse for advice, which is then sent by text or email.

This paper presents a within trial, economic evaluation from the perspective of the National Health Service (NHS) of data collected during the HITS Trial.[6] This was a trial of a telemonitoring-based service redesign compared with usual care for the management of uncontrolled hypertension which was powered to detect differences in mean systolic BP but also collected resource use data as a secondary outcome. The analysis presented here, while not part of the trial protocol, was conceived prior to completion of the primary clinical analysis for the trial.

Methods

Overview of the HITS Trial

This was a six-month pragmatic, prospective, parallel-group randomised controlled trial with blinded outcome assessments. 401 patients were recruited from 20 practices representing a range of socio-economic diversity including the 5th most deprived and second most affluent in Lothian, Scotland.

Participants were included in the study if their daytime ambulatory BP averaged ≥135/85mmHg and <210/135mmHg measured by the Spacelabs 90207 Ambulatory Blood Pressure Monitor (ABPM).[7] Exclusion criteria were inability to consent, atrial fibrillation, being on the stroke or diabetes registers (as these patients would be invited to other trials in our portfolio of trials investigating the role of telemonitoring in the management of long-term conditions), treatment for cardiac event or other life-threatening illness within the past six months, major surgery within the last three months, renal failure, or hypertension not managed in primary care. A full list of baseline measurements can be found in Table 1.

Patients were randomised in a 1:1 ratio either to the telemonitoring intervention or usual care using a secure randomisation system provided by the Edinburgh Clinical Trials Unit with minimisation on the basis of age, sex, family practice, use of three or more hypertension drugs and self-monitoring history. Because simple minimisation within centres can lead to alternation of treatment allocation and potential loss of allocation concealment, a degree of random allocation was also incorporated.

Research nurses gave patients assigned to the intervention a training session on how to use the telemonitoring equipment. As the intervention comprised providing telemetric equipment, neither participants nor investigators could be masked to group assignment.

Participants were asked to monitor their own BP twice each morning and twice each evening for the first week and then at least weekly thereafter or as often as they wished. They used a validated automated sphygmomanometer (Stabil-O-Graph® mobil, IEM, Germany).[8] This linked via Bluetooth® connection to a mobile phone, which automatically transmitted readings to a central server managed by IEM Ltd (Stuttgart, Germany). Patients and clinicians could log on to a website to see the data and automated SMS texts/emails could be sent to patients informing them of the level of their control (see Box 1 for a fuller description of the process). Patients could contact clinicians if they were concerned about their BP control and clinicians could contact patients if needed to arrange modification of therapy where required. The target home-monitored BP was <135/85mmHg based on contemporaneous UK guidelines,[9] subsequently endorsed by the National Institute for Health and Clinical Excellence (NICE).[10]

Patients allocated to the usual care arm were told that the ABPM showed that their BP was uncontrolled and that they should see their GP/practice nurse for further management, but otherwise they received standard care for hypertension from their GP or nurse who were

asked to aim for a target surgery BP of <140/90mmHg based on UK guidelines (current at the time).[9]

In order to maintain blinding of outcome assessment, patients were asked not to reveal their treatment group allocation to the research nurse undertaking the assessment; however it is not possible to rule out unblinding where patients did not adhere to this.

Cost estimation

Mean costs per patient were estimated from an NHS perspective. The trial collected data the number of consultations with a general practitioner (GP), practice nurse or district nurse (separately for practice, telephone or home visits), NHS24 (emergency out-of-hours telephone helpline) contacts, out-of-office consultations with the Lothian Unscheduled Care Service (LUCS) and accident and emergency (A&E) visits. These were collected at follow up by a research nurse with access to patient records. If the patient did not attend follow up, but agreed for the data to be collected, the research nurses completed the data from the records in their absence. Data on each drug issued to each patient, the dose per day, and the number of days issued were taken from GP records from randomisation until six months after randomisation. Drugs were assumed to be the lowest cost generic treatment which matched the daily dosing structure recommended in the British National Formulary (BNF)[11] unless a specific brand was stated. Assumptions were made on an ad-hoc basis blind to treatment allocation for the 2.4% of drug entries where doses and drug combinations failed to match perfectly to the recommended dosing structure.

Unit costs were applied to each item. Where possible, these were taken from recognised national sources.[12-18] The base year for costs was the financial year 2009/10. Any estimates from different years were inflated/deflated using an appropriate inflation index (See Table 2). With the exception of equipment costs (see Table 3), discounting was not required as the trial was less than one year in duration.

A detailed breakdown of the interventions costs of six months of BP telemonitoring, assumptions made in their estimation, price weights applied, inflation indices used and their sources is given in Table 3. The price of the full six months of intervention was applied uniformly to all patients in the monitored group, regardless of whether or not they completed the trial.

Although data were also collected on the number of hospital admissions attended by each patient during the trial, the cost of hospital admissions can vary substantially depending on the nature of the admission[15,19] and specific details of the nature of each admission were not recorded. Instead, reported admissions were matched with entries in the adverse events log for the trial to generate verbal descriptions of each event. BM viewed the extracted descriptions of each event blind to randomisation allocation, assigned Healthcare Resource Group (HRG4) codes based on the descriptions and assessed whether the event could be at least be possibly related to BP management. HRG4 codes are used in the NHS to group procedures into categories of hospital care which incur similar resource use.

Of the 28 admissions recorded in the adverse events log seven (25%) were for cardiovascular related diagnoses and as such were deemed indirectly related to high blood pressure or related to dizziness or falls for which blood pressure could not be ruled out as a contributing factor. None could specifically be related to telemonitoring itself. The decision therefore was made not to include these costs in the base case analysis as there was a risk of overwhelming the more robust estimates of other cost factors with unreliable, and likely unrelated, admission costs. However, a sensitivity analysis was undertaken including the costs of hospital admissions where price weights were applied from the Scottish National Tariff[19] based on the HRG4 code selected.

Effect variable

The effect variable for the cost-effectiveness analysis was mean daytime systolic ambulatory blood pressure (SABP). For both groups this was measured using a Spacelabs 90207 Ambulatory Blood Pressure Monitor. We therefore calculated cost per mmHg systolic BP reduced over the six months intervention period.

Analysis

All analyses were undertaken on an intention-to-treat basis.

Missing data

Primary outcome data were missing for 11.5% of patients including 20 participants (six in the intervention group and 14 in the usual care group) were either lost to follow-up or who

withdrew consent. Economic variables were missing for 0 to 8.7%. In total 21.9% of patients had missing data for at least one variable of interest. Multiple imputation by chained equations[20] was used to create 10 imputed datasets by imputing incomplete variables under fully conditional specification. This was based on age, sex, body mass index (BMI), BP (systolic and diastolic), number of hypertension drugs, cholesterol, exhaled per cent carbon monoxide, blood HbA1c, Euroqol-5D(EQ-5D) responses and all healthcare resource use variables. Calculations were undertaken in STATA 12 using the "mi ice" command. Normally distributed parameters (including primary outcome data) were imputed using multiple regression by ordinary least squares; ordered categorical variables were imputed using ordinal logistic regression and other non-normal variables imputed using predictive mean matching. Model parameters were then estimated using the respective regressions techniques described below. These estimates and their standard errors were combined using Rubin's rules.[21]

Cost analysis

Univariate analysis was undertaken of differences between trial arms in terms of total costs and each cost sub-element. As the cost data were non-normally distributed with a heavy right skew and long tail, testing was performed using non-parametric bootstrap of differences in mean patient costs between trial arms and bias corrected confidence intervals and p-values (two tailed) were reported for each cost item with significance set at the 5% level.

Cost-effectiveness analysis

Baseline resource use was not recorded. We would expect randomisation to balance out baseline costs between groups. However to counteract any baseline imbalances, point estimates for incremental costs were estimated using a generalised linear model (GLM) controlling for age, sex, baseline systolic BP and baseline health related quality of life (calculated by baseline EQ-5D index score[22]). GLMs allow adjustments to be made for heteroscedasticity and skew by the adoption of a 'family' and link function.[23,24]

Family function was selected by Modified-Parks test[24] and a power function for the link was selected on the balance of p-values from three tests of fit as recommended by Glick et al.[23] These tests were, the Modified Hosmer & Lemeshow test (tests for systematic bias in fit on raw scale), the Pregibon link test (tests for linearity of response on scale of estimation), and

Pearson correlation test (tests for systematic bias in fit on raw scale). The Gaussian family was selected and a power of 0.5343 was selected for the link function.

For incremental BP point reduction, multiple regression (by ordinary least squares) was used controlling for baseline SABP and all minimisation variables namely: age; sex; general practice; use of three or more hypertension drugs and self-monitoring history. This was selected for its equivalence to the analysis used for the variable in the primary analysis.[6]

Incremental cost-effectiveness ratios (ICERs) were expressed as cost per 1 mmHg systolic BP point reduced. Bias-corrected confidence intervals[25] for the ICERs were estimated from the bootstrapped data generated using the "recycled predictions" method as described by Glick et al.[23] This technique generates a large number of bootstrapped samples (10,000 replications were used). The chosen regressions for each variable were used to estimate incremental costs, BP and their respective ICERS within each sample.

The proportion of samples in which the intervention is shown to be cost-effective to the NHS at a given price per mean systolic mmHg (using the net benefit technique[26]) is used to estimate the probability that the intervention is cost-effective at that price. The process was repeated varying the price over a range between £0 and £100 per systolic mmHg to plot cost-effectiveness acceptability curves (CEACs). CEACs show the probability the treatment is cost-effective at varying costs (willingness on behalf of the NHS to pay) per unit of outcome (1 mmHg systolic BP reduced) to a decision maker.

As several assumptions were made in the intervention costs (see Table 3), as a sensitivity analysis, CEACs were calculated with the total cost of six months of intervention varied in increments of 25% to +/- 100% of the base case price (See Figure 3).

Results

Analysis of costs

Table 4 details the results of the univariate analysis of costs and resource use per patient associated with each trial arm. The mean total estimated healthcare cost per patient was £287.18 in the intervention group and £177.95 the usual care group (mean difference £109.23, 95% CI £76.36 to £140.63) in univariate analysis. Controlling for baseline

characteristics in the multivariate analysis gave similar results with a mean total costs of £290.13 in the intervention group and £174.81 in the usual care group (mean difference £115.32, 95% CI £83.49 to £146.63).

The difference in total costs remained significant with the cost of the telemonitoring technology excluded from the analysis demonstrating that NHS costs rose outside of the cost of the intervention itself. This was driven largely by a significant increase in mean costs arising from approximately one additional GP surgery consultation and half a practice nurse surgery consultation per person in the intervention group compared with the usual care group. The only other significant cost element difference was approximately half an additional practice nurse phone consultation. No other cost element was significantly different between the groups. This included the cost of prescribed medication. Despite a significantly greater increase in the doses of prescribed medication in the telemonitored group over that of the usual care group,[6] the rise in cost was relatively trivial as often higher strength medications were priced similarly to lower strengths.

In sensitivity analysis, the mean cost of hospital admissions in the intervention arm were £287.01 compared with £181.54 in the control arm (mean difference £105.47, 95% CI £-123.16 to £402.40; p=0.424) which raises the mean difference in total NHS costs to £214.70 (95% CI £-23.71 to £526.65; p=0.098). However, this estimate was dominated by one patient in the intervention arm with admissions costing over £17,000, none of which were assessed to be possibly related to blood pressure management. When the costs of these admissions of this patient were excluded, the equivalent mean differences in hospital costs fell to £16.56 (95% CI £-188.04 to £202.17; p=0.846) and total costs to £125.79 (95% CI £-88.85 to £318.40; p=0.223).

Analysis of blood pressure point reduction

Following imputation, the mean daytime SABP fell in both groups, from 146.20mmHg to 140.15mmHg in the telemonitoring arm and 146.22mmHg to 144.50mmHg in the usual care arm. The difference in mean daytime SABP at six months between the two arms (i.e. control-telemonitoring) was 4.51 mmHg (95%CI 2.49 to 6.61; p<0.001), adjusted for baseline mean daytime SABP and minimisation factors.

Cost-effectiveness analysis

Figure 2 shows the joint distribution of incremental costs and incremental systolic blood pressure point reduction generated by the bootstrap replicates. In all replicates, costs per patient were higher and mean SABP per patient was lower in the monitored group than the control ($p<0.001$ for both variables). This indicates that the telemonitoring was both more costly and more effective than usual care in all replicates. The ICER was £25.60/mmHg (95% CI £16.05 to £46.69).

Figure 3 shows the probability of telemonitoring being cost-effective at varied NHS willingness to pay per BP point reduction. The 100% line represents the base case analysis with intervention costs at £70.77 and the other lines showing how the CEAC would change if intervention costs were higher or lower.

Discussion

Over the six months of the trial, the intervention was significantly more effective than usual care, but also significantly more costly, on average lowering SABP by 4.51mmHg and raising total cost by £115.32. The increase in costs was predominantly driven by the estimated intervention costs (£70.77) and increased costs associated with telemonitored patients using on average approximately one additional GP surgery consultation and half a practice nurse surgery consultation. Although telephone consultations with the practice nurse and their costs also significantly rose (by approximately half a call on average), the costs for these were relatively small and had little impact on total cost.

The trial found a significant increase in the dosages of medication issued[6] which may explain some of the additional consultations as they were likely to have been required for prescribing and monitoring of patients during transition to a new drug/dose. Interestingly however medication costs did not rise significantly in spite of this intensification. This is due to higher dosage pills often costing less per dose than lower dosage pills when costs of generic treatments are used for these estimates.[16] There is a risk that the way in which the medication costs were estimated (selecting a generic where available and selecting the lowest cost option that matched dosing recommendations[11]) could have contributed substantially to this finding. However, such an approach does at least attempt to estimate the difference in costs attainable under best practice assuming this includes the selection of the lowest cost drug based on active agent.

It should be noted that our accompanying qualitative study[27] suggests that over the trial, clinicians found face-to-face communication with patients was not necessary to support BP telemonitoring and that they substituted some of these forms of consultation with other modes of communication: mainly telephone and on two occasions email. Both patients and clinicians thought that in the longer-term BP telemonitoring would reduce the need for surgery visits. Thus a reduction in the GP consultations element of the overall costs may be realised in the longer-term. This has been found in previous studies of telemonitoring where consultation costs were lower.[28,29,30]

The remaining cost elements were also non-significantly different between groups and played relatively minor roles in the overall total cost differences.

In sensitivity analysis, hospital costs were non-significantly higher on average in the intervention group than in the control by £105.47 raising differences in mean total costs to £214.70. However differences in costs of hospital admissions were exaggerated by the inclusion of an outlier patient in the intervention arm unrelated to blood pressure management. With these excluded, hospital costs were similar in both arms with an insignificant difference of £16.56. In both cases uncertainty surrounding hospital cost dominated uncertainty surrounding total cost figures. Hence when hospital admissions are included in total costs estimates we are no longer confident that the cost of resource use outside of the intervention service itself was higher or lower in the intervention group because secondary care costs have the potential for the largest financial impact on the NHS. However there are strong reasons to doubt that any of the hospital admissions observed during the trial were related to the patient's current BP, even those of a cardiovascular nature. This is because it is possible that events resulting in hospital admission may well have been set in motion prior to the onset of the study though we lack data to confirm this either way. A recent meta-analysis also found no link between home blood pressure telemonitoring and short term rates of adverse events.[28]

Dividing per patient mean differences in costs by per patient mean differences in blood-pressure reduction yields an ICER of £25.56/mmHg. Whilst on the face of it modest, there are to our knowledge no criteria available to assess the cost-effectiveness of the value of a BP point reduction, hence no formal assessment of whether this constitutes evidence that the intervention is cost-effective or not can be offered. It should also be recognised that £25.56/mmHg is a ratio rather than a tariff. It is perhaps more accurate to say that over the

first 6 months of the intervention we estimate that BP will reduce on average by 4.51 mmHg at a cost of around £115.32 per patient.

It is not known if the improved BP control found in the trial would be sustained once telemonitoring ceased. However, If sustained over 10 years, this type of reduction would be expected to lead to a >15% reduction in risk of stroke and >10% reduction in risk of coronary heart disease.[31] The costs incurred in the intervention period were low relative to the several thousand pounds likely to be spent on a cardiovascular event.[15,19,32] For example, Youman et al[32] calculated the cost of a stroke to the NHS in 2001 to be £15,306 over five years. Should the blood-pressure point reduction be sustained beyond the observed six months examined here, the expected reduction in cardiovascular events[31] may mean that that the intervention is dominant over usual care in the long term, that is to say both more effective and cost saving. Estimating this would require a study with a much longer follow-up or, perhaps more realistically, mathematical modelling of longer-term health costs and benefits. Longer term follow up of the participants is planned to determine the extent to which the difference in systolic BP persists after the end of the trial, which will be vital data to underpin such modelling.

Strengths and limitations

Unlike many previous studies, we used ABPM to measure BP. This is a considerable strength as ABPM is considered the gold standard for BP measurement and lends greater generalisability to the results as it is now recommended practice in the UK to diagnose high BP with ABPM.[10] The generalisability is further strengthened by the pragmatic setting, intention to treat analysis, the broad socioeconomic profile of participants and the absence of restrictions on participant age (oldest patient was 95) or exclusion on the basis of maximal treatment. The results may be less generalisable outside of a UK context as this is beyond the scope of this analysis.

The analysis was not part of the original trial protocol. It was however conceived prior to commencing the primary clinical analysis the usual limitations of post hoc analysis are less relevant. This did however mean that the cost analysis was restricted by the variables available in the dataset and that some cost elements have not have been accounted for, most notably outpatient visits. On the other hand, the variables that were collected were

similar to those used in other trials and are likely to be robust as surveys were completed with access to medical records.

It was not possible to control for baseline cost in multivariate analysis as these were not recorded. Instead, the analysis relies on baseline SABP and health related quality of life and on the randomisation process in its place. While it is possible that a different result may have been observed should baseline costs have been available for use, we do not anticipate that this would have differed considerably from the results presented here as it is not unreasonable to expect both of these factors to be highly correlated with baseline costs. Selection bias is very unlikely to have occurred during the randomisation/minimisation process as this service was provided remotely by clinical trials unit.

It was not possible to determine if £25.56 per mmHg reduced would be considered cost-effective or not. Using the NICE criteria for cost-effectiveness, the value of interventions are interpreted in terms of long term cost per quality adjusted life year (QALY) gained.[33,34] The EuroQol EQ-5D survey from which QALYs can be calculated[22] was included in the trial.[6] However, without sufficient power or follow-up to detect major cardiovascular events, differences in quality of life observed in the trial period would be unlikely to manifest themselves in an asymptomatic condition. Moreover, given that the participants were not blind to the intervention this might be open to bias. Hence QALYs could not reliably be estimated in this context. They are arguably better left to be determined by longer term modelling.

Comparisons to similar studies

Caution is advised when comparing studies of telemonitoring as the services within which the telemonitoring is nested often vary substantially and it is the combined effect of the telemonitoring and other interrelated services which are observed.

Two recent systematic reviews of BP telemonitoring, found few studies which included measures of healthcare utilisation and/or cost. Of those which did, office visits are frequently the only health care resource considered outside of the direct cost of the technology issued[28,35] and none were based in a UK setting, though a UK study by McManus et al suggests that an accompanying cost-effectiveness analysis is forthcoming.[29]

Meta-analyses of home BP telemonitoring versus usual care by Omboni et al 2012 find home BP telemonitoring to be associated with increased medication use, reduced office visits and

increased overall healthcare costs, though medication use and overall healthcare casts suffered from heterogeneity between studies.[28] While the increased prescribing is in line with our own findings, the decreased office visits are not. As a result Omboni et al attribute the rise in healthcare costs to the cost savings in terms of office visits being more than offset by equipment costs where our findings suggest an increase in both.[28]

An explanation for this disparity may come from the heterogeneity of the services being delivered alongside the telemonitoring. For example, McManus et al. showed that adding a medication self-titration plan to BP telemonitoring produced similar reductions in BP to our study, but found no increase in face to face consultations with physicians.[29] This lends strength to the possibility that many of the increased GP surgery visits observed in this trial were required for prescribing.

Comparisons of healthcare costs with studies outside of the UK can also be problematic as different social insurance systems jeopardise cross-border generalisability, indeed Omboni et al attribute the heterogeneity in their analysis of healthcare costs to this issue.[28]

Madsen et al compared the cost-effectiveness of a similar intervention with usual care from a Danish health service perspective.[30] In contrast to our findings, they found higher consultation and medication costs in their control arm. Again these were more than offset by equipment costs leaving total costs significantly higher in the intervention arm however SABP was non-significantly higher in the intervention arm by 2.8mmHg. The authors attribute the raised medication costs to significantly increased prescribing of AT2-antagonists in the control arm. This intensification in prescribing in the usual care group rather than the intervention group as in our trial may go some way to explaining the lower reduction in blood pressure observed. However the fact that point estimates for SAPB improvement in Madsen et al's study were still in favour of the intervention suggests that medication prescribing may not be the only factor influencing BP.

Conclusions

In conclusion, although more expensive to the NHS than usual care, telemonitoring of BP in primary care was more effective at reducing blood pressure during the 6 months of intervention. These costs may be recuperated in the long term as a result of prevention of future cardiovascular events if the reduction in BP is maintained. Further research is

required to determine if the BP improvement is sustained and, if so, what impact this has on cost-effectiveness.

Footnotes

Contributors: Brian McKinstry, Janet Hanley, Sarah Wild, Claudia Pagliari and Paul Padfield designed the trial. Janet Hanley and Brian McKinstry led lead the research. Mary Paterson was trial manager, Steff Lewis planned and supervised the statistical analysis, Ashma Krishan carried out the statistical analysis, Andrew Stoddart carried out the economic analysis and wrote the first and subsequent drafts of the paper, Aziz Sheikh provided advice throughout the trial. All authors critically revised the drafts and have approved the submission of the final paper.

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Competing interests: All authors have completed the Unified Competing Interest form atwww.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work

Ethical approval: The study was approved by Lothian Research Ethics Committee REC reference number: 08/S1101/38. Written informed consent was obtained from all participants.

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Data sharing: We are happy to share de-identified data with other researchers on application to the corresponding author. In addition to the data reported in this article we have patient acquired blood pressure data during the period of the study

Box 1: Description of the telemonitoring intervention (See web supplemental files for illustrations)

The intervention:

The practices and participants were asked to use a system which comprised a validated electronic home BP monitor and mobile phone technology that enabled the transfer of BP readings via SMS to a secure website which was accessible to the user and their doctor or nurse, and also provided automated feedback to the patient. The BP monitor linked to a mobile phone wirelessly, via Bluetooth. The components of the intervention were:

Home BP monitoring: Participants were asked to record their BP as agreed with the healthcare team, or more frequently as they wished. Guidance was initially to record BP twice in the morning and twice in the evening for a week in line with the European guideline on BP monitoring,[36] to build a baseline average. Thereafter, they were asked to take weekly measurements preferably at different times of day if their average BP was within the recommended range, but if they had made any lifestyle or medication change which would impact on their BP, they were asked to measure their BP for a more intensive period of monitoring to allow the rolling average to change and to more quickly assess the effect.

Transmission of data: This simply required the phone to be switched on and to have a signal when the BP measurement was taken. Participants just had to apply the cuff and press a button on the BP monitor. The reading and transmission occurred automatically. Mobile phone problems did not lead to loss of data because all readings were stored in the monitor and any un-transmitted readings were sent when the next reading was taken.

Feedback to patient participants (closed loop feedback): In addition to optionally accessing their BP record on-line, participants could also opt to receive reports via text message or email. These gave advice on the current status of their BP based on the average of the last 10 readings, and whether they should contact their doctor or nurse. Reports were generated every 10 readings or weekly, whichever was sooner, with a reminder to check BP if this had not been done. These reports could reassure them that their average BP was within target (<135/85mmHg)or tell them that their BP average was improved on the last report but not yet to target and to maintain current therapy, or that their BP was not at target and that they should contact their clinician. If an individual BP reading was very high (>220/120mmHg) an immediate text or email report was generated reinforcing the written advice in the patient information leaflet to rest for 30 minutes, check again and contact the practice if BP remained very high.

Sharing the readings with the healthcare team: Members of the healthcare team were able to access the records of their patients online via a secure login to a summary screen which listed their patients, their average BP over the last 10 readings, and the date of their last reading. Average BPs outside the recommended limits (set at 135/85mmHg for the study) were highlighted. Clicking on the each individual patient led to lists or graphs of all their readings. Clinicians could then check their patients' electronic GP record to see if there had been recent advice regarding medication or lifestyle change and if not, could contact the patient to make a change. Clinicians were recommended to check the website weekly, but the frequency of log-on could be chosen by them.

Usual Care

Participants allocated to the usual care group were asked to continue to attend the practice for BP checks according to the usual routine of the practice. If they were already home monitoring they were not discouraged from continuing.

All participants

For all participants the GP/practice nurse were informed that the ambulatory monitoring used to screen for eligibility for the HITS trial had shown that their average BP was above the target range, but they were not given the actual reading. All participants were given an information pack containing a range of publicly available leaflets on hypertension management and lifestyle modification.

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Table1. Baseline characteristics for full dataset

Variable		Monitored (N=200)	Control (N=201)
Age (Years) Mean (SD)		60.5 (11.8)	60.8 (10.7)
Male N (%)		117 (58.5)	120 (59.7)
Blood pressure self-monitoring history N (%)			
Never		128 (64.0)	126 (62.7)
Occasionally		56 (28.0)	56 (27.9)
Regularly		16 (8.0)	19 (9.5)
Body-mass index (kg/m^2) Mean (SD)		30.1 (5.7)	30.2 (6.2)
Smoking N (%)			
Yes		23 (11.5)	20 (10.0)
Mean (SD) (cigarettes/day)		17.6 (9.2)	14.9 (10.4)
No		177 (88.5)	181 (90.0)
Alcohol use[i] N (%)			
Yes		158 (79.0)	159 (79.1)
Median (1st, 3rd Quartile)[units of alcohol(10mls)/day]		1.7 (0.9, 2.9)	2.0 (0.7, 4.0)
No		37 (18.5)	41 (20.4)
Exhaled Carbon Monoxide category N (%)			
Non-smoker (1-6)		177 (88.5)	179 (89.1)
Light smoker (7-10)		0 (0.0)	3 (1.5)
Moderate smoker (11-20)		8 (4.0)	11 (5.5)
Heavy smoker (20+)		15 (7.5)	8 (4.0)
Cholesterol level (mmol/L)[ii] Mean (SD)		5.5 (1.0)	5.3 (1.0)
HbA1c level (mmol/mol)[iii] Mean (SD)		37.7 (6.5)	37.7 (5.4)
Urinary Sodium/CreatinineRatio[iv] Mean (SD)		9.7 (5.4)	10.9 (8.7)
Surgery measured Systolic BP (mmHg) Mean (SD)		152.9 (15.1)	152.4 (14.3)
Surgery measured Diastolic BP (mmHg) Mean (SD)		92.1 (11.5)	89.9 (11.3)
Daytime Ambulatory Systolic BP (mmHg) Mean (SD)		146.2 (10.6)	146.2 (10.5)
Daytime Ambulatory Diastolic BP (mmHg) Mean (SD)		87.1 (10.0)	85.4 (9.6)
HADS[29] Anxiety Score[v] Mean (SD)		5.0 (2.9)	5.1 (3.6)
HADS Depression Score[v] Mean (SD)		2.8 (2.4)	2.9 (2.5)
Exercise Tolerance Score[35vi] Mean (SD)		7.8 (2.9)	7.6 (3.0)
Stanford Self Efficacy Questionnaire (short version)[36vii] Mean (SD)		8.7 (1.4)	8.5 (1.4)
Morisky Medication Adherence Scale[37] N (%)			
Sometimes forgets to take medication[viii]:	Yes	61 (30.5)	63 (31.3)
	No	132 (66.0)	132 (65.7)
Sometimes careless about taking medication[ix]:	Yes	24 (12.0)	23 (11.4)
	No	169 (84.5)	173 (86.1)
Sometimes stops taking medication when feels better[x]:	Yes	11 (5.5)	15 (7.5)
	No	181 (90.5)	180 (89.6)
Sometimes stops taking medication when feels worse[xi]:	Yes	18 (9.0)	22 (10.9)
	No	170 (85.0)	173 (86.1)
Number of defined daily doses of hypertension drugs Median (1st, 3rd Quartile)		1.5 (1, 3)	1.7 (1, 3)
EuroQol-5D[23xii] Mean (SD)		0.875 (0.177)	0.857(0.220)

Missing data-[i]5 in Monitored & 1 in Control group.[ii]5 in Monitored & 8 in Control group. [iii]7 in Monitored & 9 in Control group. [iv]4 in Monitored & 2 in Control group. [v]2 missing in each group. [vi]1 in Monitored & 2 in Control group. [vii]6 in Monitored & 1 in Control group. [viii]6 in Monitored & 7 in Control group. [ix]5 in Monitored & 7 in Control. [x]6 in Monitored & 8 in Control. [xi]6 in Monitored & 12 in Control group. [xii] 5 in Monitored and 6 in Control group

Table2. Price weights, calculations and sources

Variable	Value		Unit	Source(s) / Notes
General Practitioner:				
Surgery	£36.00	per	consultation	[12]
Home	£120.00	per	consultation	[12]
Phone	£22.00	per	consultation	[12]
Practice Nurse:				
Surgery	£12.00	per	consultation	[12]
Home	£20.00	per	consultation	[12]
Phone	£4.74	per	consultation	Cost per hour[12] x Average Call length[13]
District Nurse:				
Surgery	£18.86	per	consultation	Cost per hour[12] x Average consultation length.[13] Consultation length assumed to be equal to that of a practice nurse.
Home	£27.00	per	consultation	[12]
Phone	£10.46	per	consultation	Cost per hour[12] x Average Call length. [13] Call length assumed to be equal to that of a practice nurse.
NHS 24 Contact	£41.71	per	contact	£35.69[14] inflated to 2009/10 prices using Hospital & Community Health Services (HCHS) pay and price inflation index[12])
LUCS Consultation	£64.82	per	consultation	Number of LUCS contacts divided by total budget, obtained private communication with NHS Lothian. Information on cost per consultation was not available.
A&E Visit	£95.00	per	visit	[15]
Medication	All medication use recorded was priced individually using the 2011 prices from the MIMS data base[16] deflated to 2009 prices using the Pharmaceutical Inflation component of the CPI[37] with adjustments made for 10.5% claw back[17] and container costs.[18]			
HBPM Service & Device	£70.77	for	6 months	Per patient. See Table3

Table 3. Price estimation and components for cost of intervention over 6 months (per patient)

Variable	Value		Unit	Source(s) / Notes
Home Blood Pressure Monitor (HBPM):				
Initial Training of Patient in Device Use	£12.00	per	patient	One off patient training in use of device. Priced as an assumed 20 minutes of practice nurse time (£36 per hour client contact[12]) based on the trial's pilot work
HBPM Device	£53.11 £1.20	per	each month*	Local pricing from manufacturer invoice (60 Euro converted to GBP using average exchange rate 2009/10[38]).
Mobile Phone	£48.48 £1.44	per	Each month*	Local pricing from internal communications with NHS Lothian telecoms (£49)) deflated from 2011 prices to 2009/10 using medical products component of CPI. [37]
Server Hosting	£0.42	per	month	Local pricing from Supplier Invoice (£1000 per year for all patients, divided by 200 patients over 12 months)
Web Hosting	£2.59	per	month	Local pricing from Supplier Invoice (3.10 Euro converted to GBP using average exchange rate 2009/10[38])
Sim Card	£1.98	per	month	Local pricing from internal communications with NHS Lothian telecoms (£2 deflated from 2011 prices to 2009/10 using medical products component of CPI[37]).
Nurse Time	£2.17	per	month	Assumption of 1 min per week of practice Nurse time spent checking incoming HBPM data (£30 per hour non-specific work[12]) based on anecdotal information.
Total**	**£70.77**	**for**	**6 months**	

* *Per month costs of HBPM Device and Mobile phone calculated using the annuity method[39] at a discount rate of 3.5% per year as recommended by NICE.[34] Assumed lifespan of device: 4 years, assumed life of mobile phone: 3 years.*

** *Total does not match sum of components due to rounding of values.*

Table4. Estimated Mean (Standard Error) Healthcare Service Resources Used And Associated Costs Per Patient By Factor

	Monitored Group (N=200)				Control Group (n=201)				Mean Cost Difference, £ (95% Confidence Interval*)		P-value*
	No. Used		*Cost, £*		*No. Used*		*Cost, £*				
GP Consultations:											
Surgery Consultations	*3.61*	*(0.19)*	*130.00*	*(7.00)*	*2.70*	*(0.21)*	*97.11*	*(7.46)*	*32.89*	*(14.55 to 51.04)*	*<0.001*
Phone Consultations	*0.57*	*(0.08)*	*12.43*	*(1.78)*	*0.49*	*(0.09)*	*10.69*	*(1.98)*	*1.74*	*(-2.74 to 6.09)*	*0.447*
Home Consultations	*0.06*	*(0.03)*	*7.74*	*(3.24)*	*0.09*	*(0.04)*	*10.39*	*(4.52)*	*-2.65*	*(-11.91 to 5.27)*	*0.553*
Total Consultations	4.24	(0.23)	150.17	(8.90)	3.27	(0.27)	118.19	(10.52)	31.97	(8.38 to 54.22)	0.004
Practice Nurse Consultations:											
Surgery Consultations	*1.90*	*(0.18)*	*22.75*	*(2.11)*	*1.41*	*(0.14)*	*16.88*	*(1.71)*	*5.86*	*(1.14 to 11.00)*	*0.016*
Phone Consultations	*0.69*	*(0.09)*	*3.28*	*(0.42)*	*0.15*	*(0.05)*	*0.71*	*(0.25)*	*2.57*	*(1.75 to 3.45)*	*<0.001*
Home Consultations	*0.02*	*(0.01)*	*0.41*	*(0.28)*	*0.01*	*(0.01)*	*0.30*	*(0.27)*	*0.11*	*(-0.38 to 0.77)*	*0.704*
Total Consultations	2.61	(0.21)	26.43	(2.27)	1.57	(0.17)	17.89	(1.88)	8.54	(3.46 to 14.15)	0.002
District Nurse Consultations	0.04	(0.02)	0.67	(0.41)	0.15	(0.11)	3.94	(3.05)	-3.26	(-11.94 to 0.39)	0.249
NHS24 Consultations	0.10	(0.03)	4.03	(1.39)	0.05	(0.02)	2.12	(0.79)	1.91	(-0.42 to 4.95)	0.139
LUCS Consultations	0.07	(0.02)	4.34	(1.39)	0.04	(0.02)	2.48	(1.16)	1.86	(-0.89 to 4.83)	0.193
Medication			24.07	(2.12)			23.59	(2.20)	0.48	(-5.83 to 6.40)	0.868
Accident and Emergency Visits	0.07	(0.02)	6.70	(2.24)	0.10	(0.03)	9.74	(2.98)	-3.04	(-8.87 to 2.47)	0.286
Subtotal Excluding Tele-monitoring			**216.41**	**(11.66)**			**177.95**	**(15.15)**	**38.46**	**(5.59 to 69.87)**	**0.019**
Tele-Monitoring Service & Device			70.77						70.77		
Total Healthcare Costs			**287.18**	**(11.66)**			**177.95**	**(15.15)**	**109.23**	**(76.36 to 140.63)**	**<0.001**

* : P-values (two-tailed) for significant difference from zero and Bias corrected confidence interval estimated by non-parametric bootstrap (10,000 replications)

LUCS : Lothian Unscheduled Care Service (out of hours GP or nurse consultations)

Figure 1. Consort Diagram

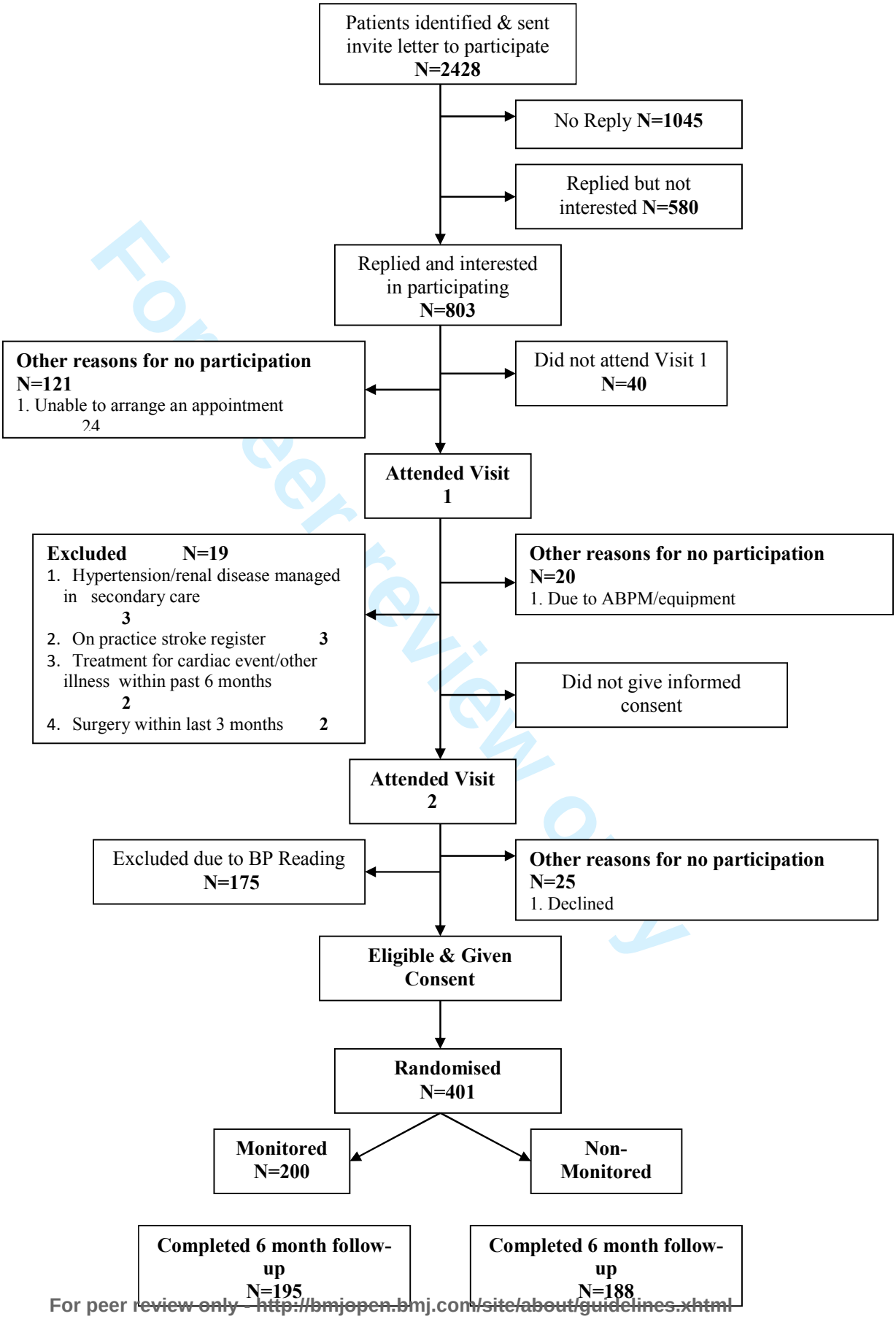


Figure 2.

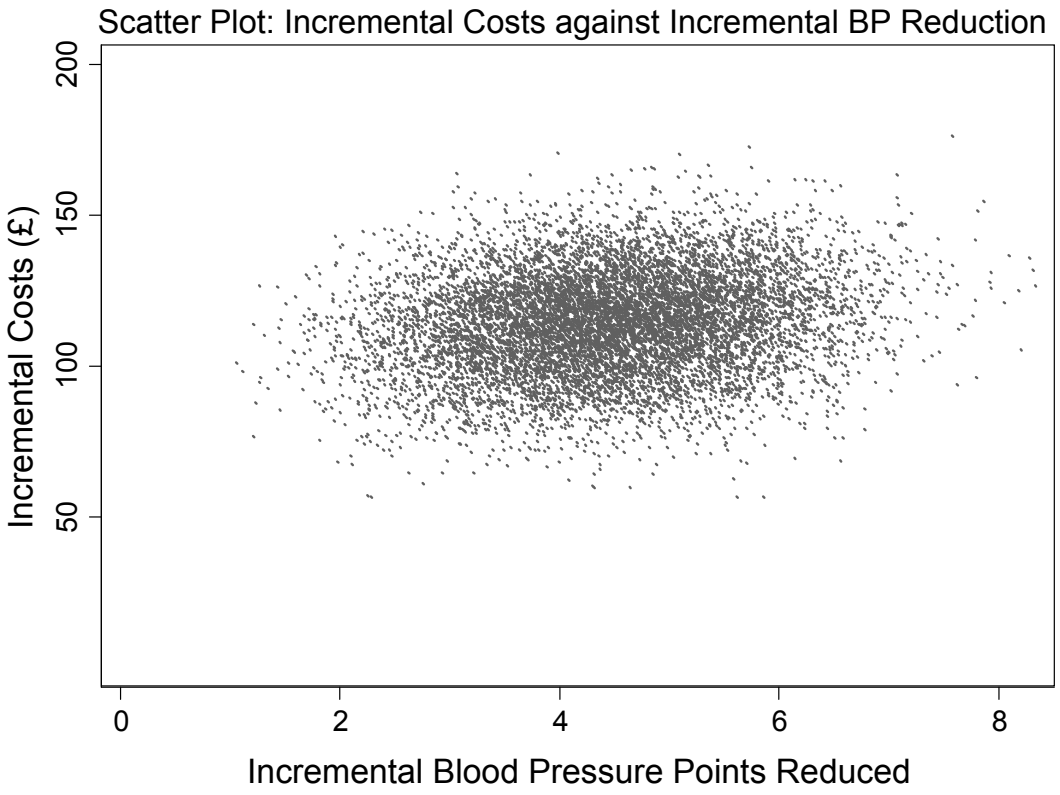
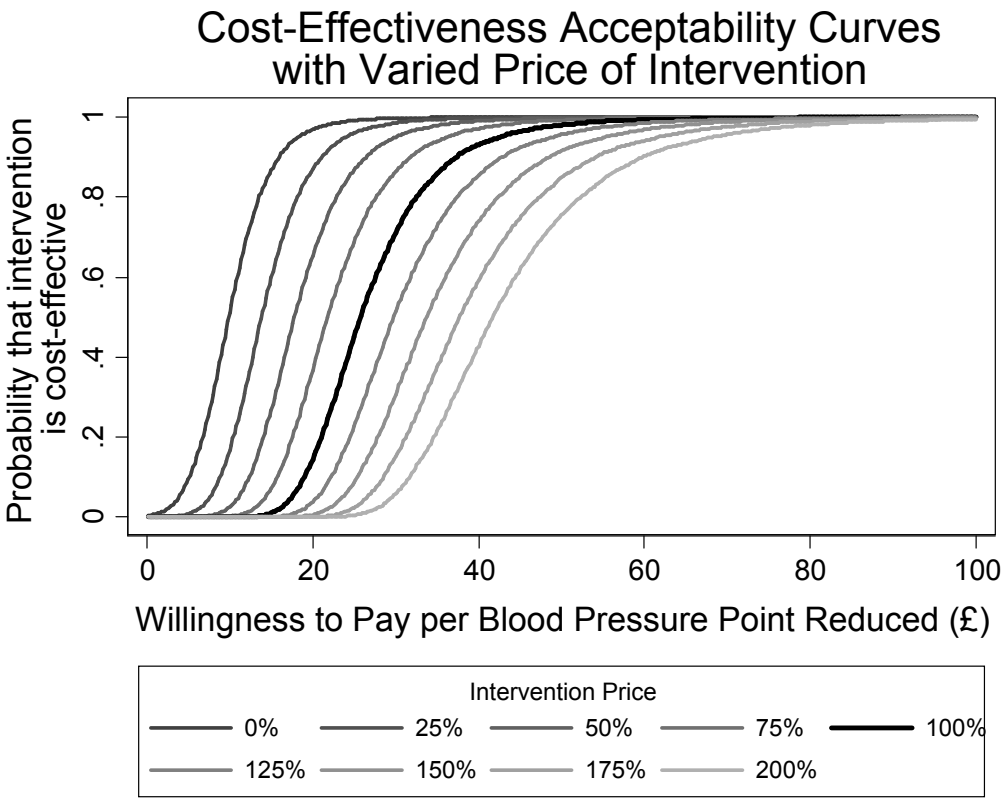


Figure 3.



Telemonitoring-based service redesign for the management of uncontrolled hypertension (HITS): Cost and cost-effectiveness analysis of a randomised controlled trial

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ABSTRACT

Objectives: To compare the costs and cost-effectiveness of managing patients with uncontrolled blood pressure (BP) using telemonitoring vs. usual care from the perspective of the National Health Service (NHS).

Design: Within trial post-hoc economic evaluation of data from a pragmatic randomised controlled trial using an intention-to-treat approach

Setting: 20 socio-economically diverse general practices in Lothian, Scotland.

Participants: 401 primary-care patients aged 29-95 with uncontrolled daytime ambulatory blood pressure (ABP) (≥135/85, but <210/135mmHg).

Intervention: Participants were centrally randomised to six months of a telemonitoring service comprising of self-monitoring of BP transmitted to a secure website for review by the attending nurse/doctor and patient, with optional automated patient decision-support by text/email (n=200), or usual care (n-201). Randomisation was undertaken with minimisation for age, sex, family practice, use of three or more hypertension drugs and self-monitoring history.

Main outcome measures: Mean difference in total NHS costs between trial arms and blinded assessment of mean cost per 1 mmHg systolic BP point reduced.

Results: Home telemonitoring of BP cost significantly more than usual care (mean difference per patient £115.32 (95% CI £83.49 to £146.63; p<0.0001)). Increased costs were due to telemonitoring service costs, patient training and additional general practitioner and nurse consultations. The mean cost of systolic BP reduction was £25.56/mmHg (95% CI £16.06 to £46.89) per patient.

Conclusions: Over the 6 month trial period, supported telemonitoring was more effective at reducing BP than usual care, but also more expensive. If clinical gains are maintained, these additional costs would be very likely to be compensated for by reductions in the cost of future cardiovascular events. Longer-term modelling of costs and outcomes is required to fully examine the cost-effectiveness implications.

Trial registration: International Standard Randomised Controlled Trials, number ISRCTN72614272.

Introduction

Hypertension is a major reversible risk factor for stroke and heart disease. It was estimated in 2001 that uncontrolled high blood pressure (BP) cost $370 billion globally (£256 billion, €413 billion) with a potential cost of $3.6 trillion (£2.5 trillion, €4.0 trillion) over a 10 year period in indirect costs.[1] Despite effective medications, BP is difficult to control for many people.[2] This is due in part to infrequent monitoring,[3] a reluctance on the part of clinicians to intensify treatment[4] and pharmacological interventions by patients.[5] Telemonitoring of BP involves patients regularly taking their own readings with onward transmission in almost real time to a website which can be accessed by themselves or by their doctor or nurse and can provide patients with decision support, in terms of when to contact a doctor or nurse for advice, which is then sent by text or email.

This paper presents a within trial, economic evaluation from the perspective of the National Health Service (NHS) of data collected during the HITS Trial.[6] This was a trial of a telemonitoring-based service redesign compared with usual care for the management of uncontrolled hypertension which was powered to detect differences in mean systolic BP but also collected resource use data as a secondary outcome. The analysis presented here, while not part of the trial protocol, was conceived prior to completion of the primary clinical analysis for the trial.

Methods

Overview of the HITS Trial

This was a six-month pragmatic, prospective, parallel-group randomised controlled trial with blinded outcome assessments. 401 patients were recruited from 20 practices representing a range of socio-economic diversity including the 5th most deprived and second most affluent in Lothian, Scotland.

Participants were included in the study if their daytime ambulatory BP averaged ≥135/85mmHg and <210/135mmHg measured by the Spacelabs 90207 Ambulatory Blood Pressure Monitor (ABPM).[7] Exclusion criteria were inability to consent, atrial fibrillation, being on the stroke or diabetes registers (as these patients would be invited to other trials in our portfolio of trials investigating the role of telemonitoring in the management of long-term conditions), treatment for cardiac event or other life-threatening illness within the past six months, major surgery within the last three months, renal failure, or hypertension not managed in primary care. A full list of baseline measurements can be found in Table 1.

Patients were randomised in a 1:1 ratio either to the telemonitoring intervention or usual care using a secure randomisation system provided by the Edinburgh Clinical Trials Unit with minimisation on the basis of age, sex, family practice, use of three or more hypertension drugs and self-monitoring history. Because simple minimisation within centres can lead to alternation of treatment allocation and potential loss of allocation concealment, a degree of random allocation was also incorporated.

Research nurses gave patients assigned to the intervention a training session on how to use the telemonitoring equipment. As the intervention comprised providing telemetric equipment, neither participants nor investigators could be masked to group assignment.

Participants were asked to monitor their own BP twice each morning and twice each evening for the first week and then at least weekly thereafter or as often as they wished. They used a validated automated sphygmomanometer (Stabil-O-Graph® mobil, IEM, Germany).[8] This linked via Bluetooth® connection to a mobile phone, which automatically transmitted readings to a central server managed by IEM Ltd (Stuttgart, Germany). Patients and clinicians could log on to a website to see the data and automated SMS texts/emails could be sent to patients informing them of the level of their control (see Box 1 for a fuller description of the process). Patients could contact clinicians if they were concerned about their BP control and clinicians could contact patients if needed to arrange modification of therapy where required. The target home-monitored BP was <135/85mmHg based on contemporaneous UK guidelines,[9] subsequently endorsed by the National Institute for Health and Clinical Excellence (NICE).[10]

Patients allocated to the usual care arm were told that the ABPM showed that their BP was uncontrolled and that they should see their GP/practice nurse for further management, but otherwise they received standard care for hypertension from their GP or nurse who were

asked to aim for a target surgery BP of <140/90mmHg based on UK guidelines (current at the time).[9]

In order to maintain blinding of outcome assessment, patients were asked not to reveal their treatment group allocation to the research nurse undertaking the assessment; however it is not possible to rule out unblinding where patients did not adhere to this.

Cost estimation

Mean costs per patient were estimated from an NHS perspective. The trial collected data ~~by survey on~~ the number of consultations with a general practitioner (GP), practice nurse or district nurse (separately for practice, telephone or home visits), NHS24 (emergency out-of-hours telephone helpline) contacts, out-of-office consultations with the Lothian Unscheduled Care Service (LUCS) and accident and emergency (A&E) visits. ~~The survey was initiated at~~These were collected at follow up by a research nurse with access to patient records. If the patient did not attend follow up, but agreed for the data to be collected, the research nurses completed the data from ~~GP~~ the records in their absence. Data on each drug issued to each patient, the dose per day, and the number of days issued were taken from GP records from randomisation until six months after randomisation. Drugs were assumed to be the lowest cost generic treatment which matched the daily dosing structure recommended in the British National Formulary (BNF)[-11] unless a specific brand was stated. Assumptions were made on an ad-hoc basis blind to treatment allocation for the 2.4% of drug entries where doses and drug combinations failed to match perfectly to the recommended dosing structure.

Unit costs were applied to each item. Where possible, these were taken from recognised national sources.[12-18] The base year for costs was the financial year 2009/10. Any estimates from different years were inflated/deflated using an appropriate inflation index (See Table 2). With the exception of equipment costs (see Table 3), discounting was not required as the trial was less than one year in duration.

A detailed breakdown of the interventions costs of six months of BP telemonitoring, assumptions made in their estimation, price weights applied, inflation indices used and their sources is given in Table 3. The price of the full six months of intervention was applied

uniformly to all patients in the monitored group, regardless of whether or not they completed the trial.

Although data were also collected on the number of hospital admissions attended by each patient during the trial, the cost of hospital admissions can vary substantially depending on the nature of the admission[15,19] and specific details of the nature of each admission were not recorded ~~in the survey~~. Instead, reported admissions were matched with entries in the adverse events log for the trial to generate verbal descriptions of each event. BM viewed the extracted descriptions of each event blind to randomisation allocation, assigned Healthcare Resource Group (HRG4) codes based on the descriptions and assessed whether the event could be at least be possibly related to BP management. HRG4 codes are used in the NHS to group procedures into categories of hospital care which incur similar resource use.

Of the 28 admissions recorded in the adverse events log seven (25%) were for cardiovascular related diagnoses and as such were deemed indirectly related to high blood pressure or related to dizziness or falls for which blood pressure could not be ruled out as a contributing factor. None could specifically be related to telemonitoring itself. The decision therefore was made not to include these costs in the base case analysis as there was a risk of overwhelming the more robust estimates of other cost factors with unreliable, and likely unrelated, admission costs. However, a sensitivity analysis was undertaken including the costs of hospital admissions where price weights were applied from the Scottish National Tariff[19] based on the HRG4 code selected.

Effect variable

The effect variable for the cost-effectiveness analysis was mean daytime systolic ambulatory blood pressure (SABP). For both groups this was measured using a Spacelabs 90207 Ambulatory Blood Pressure Monitor. We therefore calculated cost per mmHg systolic BP reduced over the six months intervention period.

Analysis

All analyses were undertaken on an intention-to-treat basis.

Missing data

Primary outcome data were missing for 11.5% of patients including 20 participants (six in the intervention group and 14 in the usual care group) were either lost to follow-up or who withdrew consent. Economic variables were missing for 0 to 8.7%. In total 21.9% of patients had missing data for at least one variable of interest. Multiple imputation by chained equations[20] was used to create 10 imputed datasets by imputing incomplete variables under fully conditional specification. This was based on age, sex, body mass index (BMI), BP (systolic and diastolic), number of hypertension drugs, cholesterol, exhaled per cent carbon monoxide, blood HbA1c, Euroqol-5D(EQ-5D) responses and all healthcare resource use variables. Calculations were undertaken in STATA 12 using the "mi ice" command. Normally distributed parameters (including primary outcome data) were imputed using multiple regression by ordinary least squares; ordered categorical variables were imputed using ordinal logistic regression and other non-normal variables imputed using predictive mean matching. Model parameters were then estimated using the respective regressions techniques described below. These estimates and their standard errors were combined using Rubin's rules.[21]

Cost analysis

Univariate analysis was undertaken of differences between trial arms in terms of total costs and each cost sub-element. As the cost data were non-normally distributed with a heavy right skew and long tail, testing was performed using non-parametric bootstrap of differences in mean patient costs between trial arms and bias corrected confidence intervals and p-values (two tailed) were reported for each cost item with significance set at the 5% level.

Cost-effectiveness analysis

Baseline resource use was not recorded. We would expect randomisation to balance out baseline costs between groups. However to counteract any baseline imbalances, point estimates for incremental costs were estimated using a generalised linear model (GLM) controlling for age, sex, baseline systolic BP and baseline health related quality of life (calculated by baseline EQ-5D index score[22]). GLMs allow adjustments to be made for heteroscedasticity and skew by the adoption of a 'family' and link function.[23,24]

Family function was selected by Modified-Parks test[24] and a power function for the link was selected on the balance of p-values from three tests of fit as recommended by Glick et al.[23] These tests were, the Modified Hosmer & Lemeshow test (tests for systematic bias in fit on raw scale), the Pregibon link test (tests for linearity of response on scale of estimation), and Pearson correlation test (tests for systematic bias in fit on raw scale). The Gaussian family was selected and a power of 0.5343 was selected for the link function.

For incremental BP point reduction, multiple regression (by ordinary least squares) was used controlling for baseline SABP and all minimisation variables namely: age; sex; general practice; use of three or more hypertension drugs and self-monitoring history. This was selected for its equivalence to the analysis used for the variable in the primary analysis.[6]

Incremental cost-effectiveness ratios (ICERs) were expressed as cost per 1 mmHg systolic BP point reduced. Bias-corrected confidence ~~intervals[22]~~ intervals[25] for the ICERs were estimated from the bootstrapped data generated using the "recycled predictions" method as described by Glick et al.[23] This technique generates a large number of bootstrapped samples (10,000 replications were used). The chosen regressions for each variable were used to estimate incremental costs, BP and their respective ICERS within each sample.

The proportion of samples in which the intervention is shown to be cost-effective to the NHS at a given price per mean systolic mmHg (using the net benefit technique[26]) is used to estimate the probability that the intervention is cost-effective at that price. The process was repeated varying the price over a range between £0 and £100 per systolic mmHg to plot cost-effectiveness acceptability curves (CEACs). CEACs show the probability the treatment is cost-effective at varying costs (willingness on behalf of the NHS to pay) per unit of outcome (1 mmHg systolic BP reduced) to a decision maker.

As several assumptions were made in the intervention costs (see Table 3), as a sensitivity analysis, CEACs were calculated with the total cost of six months of intervention varied in increments of 25% to +/- 100% of the base case price (See Figure 3).

Results

Analysis of costs

Table 4 details the results of the univariate analysis of costs and resource use per patient associated with each trial arm. The mean total estimated healthcare cost per patient was £287.18 in the intervention group and £177.95 the usual care group (mean difference £109.23, 95% CI £76.36 to £140.63) in univariate analysis. Controlling for baseline characteristics in the multivariate analysis gave similar results with a mean total costs of £290.13 in the intervention group and £174.81 in the usual care group (mean difference £115.32, 95% CI £83.49 to £146.63).

The difference in total costs remained significant with the cost of the telemonitoring technology excluded from the analysis demonstrating that NHS costs rose outside of the cost of the intervention itself. This was driven largely by a significant increase in mean costs arising from approximately one additional GP surgery consultation and half a practice nurse surgery consultation per person in the intervention group compared with the usual care group. The only other significant cost element difference was approximately half an additional practice nurse phone consultation. No other cost element was significantly different between the groups. This included the cost of prescribed medication. Despite a significantly greater increase in the doses of prescribed medication in the telemonitored group over that of the usual care group,[6] the rise in cost was relatively trivial as often higher strength medications were priced similarly to lower strengths.

In sensitivity analysis, the mean cost of hospital admissions in the intervention arm were £287.01 compared with £181.54 in the control arm (mean difference £105.47, 95% CI £-123.16 to £402.40; p=0.424~~2~~) which raises the mean difference in total NHS costs to £214.70 (95% CI £-23.71 to £526.65; p=0.098~~2~~). However, this estimate was dominated by one patient in the intervention arm with ~~repeated~~ admissions ~~for the treatment of an infected wound and related scare tissue~~ costing over £17,000, none of which were assessed to be possibly related to blood pressure management. When the costs of these admissions of this patient were excluded, the equivalent mean differences in hospital costs fell to £16.56 (95% CI £-188.04 to £202.17; p=0.84~~5~~6) and total costs to £125.79 (95% CI £-88.85 to £318.40; p=0.223~~2~~).

Analysis of blood pressure point reduction

Following imputation, the mean daytime SABP fell in both groups, from 146.20mmHg to 140.15mmHg in the telemonitoring arm and 146.22mmHg to 144.50mmHg in the usual care arm. The difference in mean daytime SABP at six months between the two arms (i.e. control-

telemonitoring) was 4.51 mmHg (95%CI 2.49 to 6.61; p<0.000~~0~~1), adjusted for baseline mean daytime SABP and minimisation factors.

Cost-effectiveness analysis

Figure 2 shows the joint distribution of incremental costs and incremental systolic blood pressure point reduction generated by the bootstrap replicates. In all replicates, costs per patient were higher and mean SABP per patient was lower in the monitored group than the control (p<0.000~~0~~1 for both variables). This indicates that the telemonitoring was both more costly and more effective than usual care in all replicates. The ICER was £25.60/mmHg (95% CI £16.05 to £46.69).

Figure 3 shows the probability of telemonitoring being cost-effective at varied NHS willingness to pay per BP point reduction. The 100% line represents the base case analysis with intervention costs at £70.77 and the other lines showing how the CEAC would change if intervention costs were higher or lower.

Discussion

Over the six months of the trial, the intervention was significantly more effective than usual care, but also significantly more costly, on average lowering SABP by 4.51mmHg and raising total cost by £115.32. The increase in costs was predominantly driven by the estimated intervention costs (£70.77) and increased costs associated with telemonitored patients using on average approximately one additional GP surgery consultation and half a practice nurse surgery consultation. Although telephone consultations with the practice nurse and their costs also significantly rose (by approximately half a call on average), the costs for these were relatively small and had little impact on total cost.

The trial found a significant increase in the dosages of medication issued[6] which may explain some of the additional consultations as they were likely to have been required for prescribing and monitoring of patients during transition to a new drug/dose. Interestingly however medication costs did not rise significantly in spite of this intensification. This is due to higher dosage pills often costing less per dose than lower dosage pills when costs of generic treatments are used for these estimates.[16] There is a risk that the way in which the medication costs were estimated (selecting a generic where available and selecting the lowest cost option that matched dosing recommendations[11]) could have contributed substantially to this finding. However, such an approach does at least attempt to estimate

the difference in costs attainable under best practice assuming this includes the selection of the lowest cost drug based on active agent.

It should be noted that our accompanying qualitative study[27] suggests that over the trial, clinicians found face-to-face communication with patients was not necessary to support BP telemonitoring and that they substituted some of these forms of consultation with other modes of communication: mainly telephone and on two occasions email. Both patients and clinicians thought that in the longer-term BP telemonitoring would reduce the need for surgery visits. Thus a reduction in the GP consultations element of the overall costs may be realised in the longer-term. This has been found in previous studies of telemonitoring where consultation costs were lower.[28,29,30]

The remaining cost elements were also non-significantly different between groups and played relatively minor roles in the overall total cost differences.

In sensitivity analysis, hospital costs were non-significantly higher on average in the intervention group than in the control by £105.47 raising differences in mean total costs to £214.70. However differences in costs of hospital admissions were exaggerated by the inclusion of an outlier patient in the intervention arm unrelated to blood pressure management. With these excluded, hospital costs were similar in both arms with an insignificant difference of £16.56. In both cases uncertainty surrounding hospital cost dominated uncertainty surrounding total cost figures. Hence when hospital admissions are included in total costs estimates we are no longer confident that the cost of resource use outside of the intervention service itself was higher or lower in the intervention group because secondary care costs have the potential for the largest financial impact on the NHS. However there are strong reasons to doubt that any of the hospital admissions observed during the trial were related to the patient's current BP, even those of a cardiovascular nature. This is because it is possible that events resulting in hospital admission may well have been set in motion prior to the onset of the study though we lack data to confirm this either way. A recent meta-analysis also found no link between home blood pressure telemonitoring and short term rates of adverse events.[28]

Dividing per patient mean differences in costs by per patient mean differences in blood-pressure reduction yields an ICER of £25.56/mmHg. Whilst on the face of it modest, there are to our knowledge no criteria available to assess the cost-effectiveness of the value of a BP point reduction, hence no formal assessment of whether this constitutes evidence that

the intervention is cost-effective or not can be offered. It should also be recognised that £25.56/mmHg is a ratio rather than a tariff. It is perhaps more accurate to say that over the first 6 months of the intervention we estimate that BP will reduce on average by 4.51 mmHg at a cost of around £115.32 per patient.

It is not known if the improved BP control found in the trial would be sustained once telemonitoring ceased. However, If sustained over 10 years, this type of reduction would be expected to lead to a >15% reduction in risk of stroke and >10% reduction in risk of coronary heart disease.[2319] The costs incurred in the intervention period were low relative to the several thousand pounds likely to be spent on a cardiovascular event.[15,19,32] For example, Youman et al[32] calculated the cost of a stroke to the NHS in 2001 to be £15,306 over five years. Should the blood-pressure point reduction be sustained beyond the observed six months examined here, the expected reduction in cardiovascular events[31] may mean that that the intervention is dominant over usual care in the long term, that is to say both more effective and cost saving. Estimating this would require a study with a much longer follow-up or, perhaps more realistically, mathematical modelling of longer-term health costs and benefits. Longer term follow up of the participants is planned to determine the extent to which the difference in systolic BP persists after the end of the trial, which will be vital data to underpin such modelling.

Strengths and limitations

Unlike many previous studies, we used ABPM to measure BP. This is a considerable strength as ABPM is considered the gold standard for BP measurement and lends greater generalisability to the results as it is now recommended practice in the UK to diagnose high BP with ABPM.[10] The generalisability is further strengthened by the pragmatic setting, intention to treat analysis, the broad socioeconomic profile of participants and the absence of restrictions on participant age (oldest patient was 95) or exclusion on the basis of maximal treatment. The results may be less generalisable outside of a UK context as this is beyond the scope of this analysis.

The analysis was not part of the original trial protocol. It was however conceived prior to commencing the primary clinical analysis the usual limitations of post hoc analysis are less relevant. This did however mean that the cost analysis was restricted by the variables available in the dataset and that some cost elements have not have been accounted for,

most notably outpatient visits. On the other hand, the variables that were collected were similar to those used in other trials and are likely to be robust as surveys were completed with access to medical records.

It was not possible to control for baseline cost in multivariate analysis as these were not recorded. Instead, the analysis relies on baseline SABP and health related quality of life and on the randomisation process in its place. While it is possible that a different result may have been observed should baseline costs have been available for use, we do not anticipate that this would have differed considerably from the results presented here as it is not unreasonable to expect both of these factors to be highly correlated with baseline costs. Selection bias is very unlikely to have occurred during the randomisation/minimisation process as this service was provided remotely by clinical trials unit.

~~Randomisation was at the level of the participant. Although this raises the possibility of clustering effects, the numbers of study participants within each practice constituted a tiny proportion of all such patients and the risk of significant contamination is therefore small. A post-hoc cluster analysis revealed a low intra-cluster correlation coefficient and did not alter the outcome, suggesting that clustering did not have a major effect. In this situation, a cluster randomised trial may have been more open to bias than a participant level randomised trial.[33]~~

It was not possible to determine if £25.56 per mmHg reduced would be considered cost-effective or not. Using the NICE criteria for cost-effectiveness, the value of interventions are interpreted in terms of long term cost per quality adjusted life year (QALY) gained.[3~~34~~,3~~54~~] The EuroQol EQ-5D survey from which QALYs can be calculated[22] was included in the trial.[6] However, without sufficient power or follow-up to detect major cardiovascular events, differences in quality of life observed in the trial period would be unlikely to manifest themselves in an asymptomatic condition. Moreover, given that the participants were not blind to the intervention this might be open to bias. Hence QALYs could not reliably be estimated in this context. They are arguably better left to be determined by longer term modelling.

Comparisons to similar studies

Caution is advised when comparing studies of telemonitoring as the services within which the telemonitoring is nested often vary substantially and it is the combined effect of the telemonitoring and other interrelated services which are observed.

Two recent systematic reviews of BP telemonitoring, found few studies which included measures of healthcare utilisation and/or cost. Of those which did, office visits are frequently the only health care resource considered outside of the direct cost of the technology issued[28,365] and none were based in a UK setting, though a UK study by McManus et al suggests that an accompanying cost-effectiveness analysis is forthcoming.[29]

Meta-analyses of home BP telemonitoring versus usual care by Omboni et al 2012 find home BP telemonitoring to be associated with increased medication use, reduced office visits and increased overall healthcare costs, though medication use and overall healthcare casts suffered from heterogeneity between studies.[28] While the increased prescribing is in line with our own findings, the decreased office visits are not. As a result Omboni et al attribute the rise in healthcare costs to the cost savings in terms of office visits being more than offset by equipment costs where our findings suggest an increase in both.[28]

An explanation for this disparity may come from the heterogeneity of the services being delivered alongside the telemonitoring. For example, McManus et al. showed that adding a medication self-titration plan to BP telemonitoring produced similar reductions in BP to our study, but found no increase in face to face consultations with physicians.[29] This lends strength to the possibility that many of the increased GP surgery visits observed in this trial were required for prescribing.

Comparisons of healthcare costs with studies outside of the UK can also be problematic as different social insurance systems jeopardise cross-border generalisability, indeed Omboni et al attribute the heterogeneity in their analysis of healthcare costs to this issue.[28]

Madsen et al compared the cost-effectiveness of a similar intervention with usual care from a Danish health service perspective.[30] In contrast to our findings, they found higher consultation and medication costs in their control arm. Again these were more than offset by equipment costs leaving total costs significantly higher in the intervention arm however SABP was non-significantly higher in the intervention arm by 2.8mmHg. The authors attribute the raised medication costs to significantly increased prescribing of AT2-antagonists in the control arm. This intensification in prescribing in the usual care group rather than the intervention group as in our trial may go some way to explaining the lower reduction in blood pressure observed. However the fact that point estimates for SAPB improvement in Madsen et al's study were still in favour of the intervention suggests that medication prescribing may not be the only factor influencing BP.

Conclusions

In conclusion, although more expensive to the NHS than usual care, telemonitoring of BP in primary care was more effective at reducing blood pressure during the 6 months of intervention. These costs may be recuperated in the long term as a result of prevention of future cardiovascular events if the reduction in BP is maintained. Further research is required to determine if the BP improvement is sustained and, if so, what impact this has on cost-effectiveness.

Footnotes

Contributors**:** Brian McKinstry, Janet Hanley, Sarah Wild, Claudia Pagliari and Paul Padfield designed the trial. Janet Hanley and Brian McKinstry led lead the research. Mary Paterson was trial manager, Steff Lewis planned and supervised the statistical analysis, Ashma Krishan carried out the statistical analysis, Andrew Stoddart carried out the economic analysis and wrote the first and subsequent drafts of the paper, Aziz Sheikh provided advice throughout the trial. All authors critically revised the drafts and have approved the submission of the final paper.

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Competing interests: All authors have completed the Unified Competing Interest form atwww.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work

Ethical approval: The study was approved by Lothian Research Ethics Committee REC reference number: 08/S1101/38. Written informed consent was obtained from all participants.

Data sharing: Anonymised datasets may be available from the corresponding author on application.

Box 1: Description of the telemonitoring intervention (See web supplemental files for illustrations)

The intervention:

The practices and participants were asked to use a system which comprised a validated electronic home BP monitor and mobile phone technology that enabled the transfer of BP readings via SMS to a secure website which was accessible to the user and their doctor or nurse, and also provided automated feedback to the patient. The BP monitor linked to a mobile phone wirelessly, via Bluetooth. The components of the intervention were:

Home BP monitoring: Participants were asked to record their BP as agreed with the healthcare team, or more frequently as they wished. Guidance was initially to record BP twice in the morning and twice in the evening for a week in line with the European guideline on BP monitoring,[3 7 6] to build a baseline average. Thereafter, they were asked to take weekly measurements preferably at different times of day if their average BP was within the recommended range, but if they had made any lifestyle or medication change which would impact on their BP, they were asked to measure their BP for a more intensive period of monitoring to allow the rolling average to change and to more quickly assess the effect.

Transmission of data: This simply required the phone to be switched on and to have a signal when the BP measurement was taken. Participants just had to apply the cuff and press a button on the BP monitor. The reading and transmission occurred automatically. Mobile phone problems did not lead to loss of data because all readings were stored in the monitor and any un-transmitted readings were sent when the next reading was taken.

Feedback to patient participants (closed loop feedback): In addition to optionally accessing their BP record on-line, participants could also opt to receive reports via text message or email. These gave advice on the current status of their BP based on the average of the last 10 readings, and whether they should contact their doctor or nurse. Reports were generated every 10 readings or weekly, whichever was sooner, with a reminder to check BP if this had not been done. These reports could reassure them that their average BP was within target (<135/85mmHg)or tell them that their BP average was improved on the last report but not yet to target and to maintain current therapy, or that their BP was not at target and that they should contact their clinician. If an individual BP reading was very high (>220/120mmHg) an immediate text or email report was generated reinforcing the written advice in the patient information leaflet to rest for 30 minutes, check again and contact the practice if BP remained very high.

Sharing the readings with the healthcare team: Members of the healthcare team were able to access the records of their patients online via a secure login to a summary screen which listed their patients, their average BP over the last 10 readings, and the date of their last reading. Average BPs outside the recommended limits (set at 135/85mmHg for the study) were highlighted. Clicking on the each individual patient led to lists or graphs of all their readings. Clinicians could then check their patients' electronic GP record to see if there had been recent advice regarding medication or lifestyle change and if not, could contact the patient to make a change. Clinicians were recommended to check the website weekly, but the frequency of log-on could be chosen by them.

Usual Care

Participants allocated to the usual care group were asked to continue to attend the practice for BP checks according to the usual routine of the practice. If they were already home monitoring they were not discouraged from continuing.

All participants

For all participants the GP/practice nurse were informed that the ambulatory monitoring used to screen for eligibility for the HITS trial had shown that their average BP was above the target range, but they were not given the actual reading. All participants were given an information pack containing a range of publicly available leaflets on hypertension management and lifestyle modification.

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Table1. Baseline characteristics for full dataset

Variable		Monitored (N=200)	Control (N=201)
Age (Years) Mean (SD)		60.5 (11.8)	60.8 (10.7)
Male N (%)		117 (58.5)	120 (59.7)
Blood pressure self-monitoring history N (%)			
Never		128 (64.0)	126 (62.7)
Occasionally		56 (28.0)	56 (27.9)
Regularly		16 (8.0)	19 (9.5)
Body-mass index (kg/m^2) Mean (SD)		30.1 (5.7)	30.2 (6.2)
Smoking N (%)			
Yes		23 (11.5)	20 (10.0)
Mean (SD) (cigarettes/day)		17.6 (9.2)	14.9 (10.4)
No		177 (88.5)	181 (90.0)
Alcohol use[i] N (%)			
Yes		158 (79.0)	159 (79.1)
Median (1st, 3rd Quartile)[units of alcohol(10mls)/day]		1.7 (0.9, 2.9)	2.0 (0.7, 4.0)
No		37 (18.5)	41 (20.4)
Exhaled Carbon Monoxide category N (%)			
Non-smoker (1-6)		177 (88.5)	179 (89.1)
Light smoker (7-10)		0 (0.0)	3 (1.5)
Moderate smoker (11-20)		8 (4.0)	11 (5.5)
Heavy smoker (20+)		15 (7.5)	8 (4.0)
Cholesterol level (mmol/L)[ii] Mean (SD)		5.5 (1.0)	5.3 (1.0)
HbA1c level (mmol/mol~~%~~)[iii] Mean (SD)		37.7 (6.5)	37.7 (5.4)
Urinary Sodium/CreatinineRatio[iv] Mean (SD)		9.7 (5.4)	10.9 (8.7)
Surgery measured Systolic BP (mmHg) Mean (SD)		152.9 (15.1)	152.4 (14.3)
Surgery measured Diastolic BP (mmHg) Mean (SD)		92.1 (11.5)	89.9 (11.3)
Daytime Ambulatory Systolic BP (mmHg) Mean (SD)		146.2 (10.6)	146.2 (10.5)
Daytime Ambulatory Diastolic BP (mmHg) Mean (SD)		87.1 (10.0)	85.4 (9.6)
HADS[29] Anxiety Score[v] Mean (SD)		5.0 (2.9)	5.1 (3.6)
HADS Depression Score[v] Mean (SD)		2.8 (2.4)	2.9 (2.5)
Exercise Tolerance Score[35vi] Mean (SD)		7.8 (2.9)	7.6 (3.0)
Stanford Self Efficacy Questionnaire (short version)[36vii] Mean (SD)		8.7 (1.4)	8.5 (1.4)
Morisky Medication Adherence Scale[37] N (%)			
Sometimes forgets to take medication[viii]:	Yes	61 (30.5)	63 (31.3)
	No	132 (66.0)	132 (65.7)
Sometimes careless about taking medication[ix]:	Yes	24 (12.0)	23 (11.4)
	No	169 (84.5)	173 (86.1)
Sometimes stops taking medication when feels better[x]:	Yes	11 (5.5)	15 (7.5)
	No	181 (90.5)	180 (89.6)
Sometimes stops taking medication when feels worse[xi]:	Yes	18 (9.0)	22 (10.9)
	No	170 (85.0)	173 (86.1)
Number of defined daily doses of hypertension drugs Median (1st, 3rd Quartile)		1.5 (1, 3)	1.7 (1, 3)
EuroQol-5D[23xii] Mean (SD)		0.875 (0.177)	0.857(0.220)

Missing data-[i]5 in Monitored & 1 in Control group.[ii]5 in Monitored & 8 in Control group. [iii]7 in Monitored & 9 in Control group. [iv]4 in Monitored & 2 in Control group. [v]2 missing in each group. [vi]1 in Monitored & 2 in Control group. [vii]6 in Monitored & 1 in Control group. [viii]6 in Monitored & 7 in Control group. [ix]5 in Monitored & 7 in Control. [x]6 in Monitored & 8 in Control. [xi]6 in Monitored & 12 in Control group. [xii] 5 in Monitored and 6 in Control group

Table2. Price weights, calculations and sources

Variable	Value		Unit	Source(s) / Notes
General Practitioner:				
Surgery	£36.00	per	consultation	[12]
Home	£120.00	per	consultation	[12]
Phone	£22.00	per	consultation	[12]
Practice Nurse:				
Surgery	£12.00	per	consultation	[12]
Home	£20.00	per	consultation	[12]
Phone	£4.74	per	consultation	Cost per hour[12] x Average Call length[13]
District Nurse:				
Surgery	£18.86	per	consultation	Cost per hour[12] x Average consultation length.[13] Consultation length assumed to be equal to that of a practice nurse.
Home	£27.00	per	consultation	[12]
Phone	£10.46	per	consultation	Cost per hour[12] x Average Call length. [13] Call length assumed to be equal to that of a practice nurse.
NHS 24 Contact	£41.71	per	contact	£35.69[14] inflated to 2009/10 prices using Hospital & Community Health Services (HCHS) pay and price inflation index[12])
LUCS Consultation	£64.82	per	consultation	Number of LUCS contacts divided by total budget, obtained private communication with NHS Lothian. Information on cost per consultation was not available.
A&E Visit	£95.00	per	visit	[15]
Medication	All medication use recorded was priced individually using the 2011 prices from the MIMS data base[16] deflated to 2009 prices using the Pharmaceutical Inflation component of the ~~CPI[38]~~ CPI[37] with adjustments made for 10.5% claw back[17] and container costs.[18]			
HBPM Service & Device	£70.77	for	6 months	Per patient. See Table3

Table 3. Price estimation and components for cost of intervention over 6 months (per patient)

Variable	Value		Unit	Source(s) / Notes
Home Blood Pressure Monitor (HBPM):				
Initial Training of Patient in Device Use	£12.00	per	patient	One off patient training in use of device. Priced as an assumed 20 minutes of practice nurse time (£36 per hour client contact[12]) based on the trial's pilot work
HBPM Device	£53.11 £1.20	per	each month*	Local pricing from manufacturer invoice (60 Euro converted to GBP using average exchange rate 2009/~~10~~[39]10[38]).
Mobile Phone	£48.48 £1.44	per	Each month*	Local pricing from internal communications with NHS Lothian telecoms (£49)) deflated from 2011 prices to 2009/10 using medical products component of CPI. [38]37
Server Hosting	£0.42	per	month	Local pricing from Supplier Invoice (£1000 per year for all patients, divided by 200 patients over 12 months)
Web Hosting	£2.59	per	month	Local pricing from Supplier Invoice (3.10 Euro converted to GBP using average exchange rate 2009/~~10~~[39]10[38])
Sim Card	£1.98	per	month	Local pricing from internal communications with NHS Lothian telecoms (£2 deflated from 2011 prices to 2009/10 using medical products component of ~~CPI~~[38]CPI[37]).
Nurse Time	£2.17	per	month	Assumption of 1 min per week of practice Nurse time spent checking incoming HBPM data (£30 per hour non-specific work[12]) based on anecdotal information.
Total**	**£70.77**	**for**	**6 months**	

* *Per month costs of HBPM Device and Mobile phone calculated using the annuity ~~method~~[40] method[39] at a discount rate of 3.5% per year as recommended by NICE.[33]4 Assumed lifespan of device: 4 years, assumed life of mobile phone: 3 years.*

** *Total does not match sum of components due to rounding of values.*

Table4. Estimated Mean (Standard Error) Healthcare Service Resources Used And Associated Costs Per Patient By Factor

	Monitored Group (N=200)				Control Group (n=201)				Mean Cost Difference, £ (95% Confidence Interval*)		P-value*
	No. Used		*Cost, £*		*No. Used*		*Cost, £*				
GP Consultations:											
Surgery Consultations	*3.61*	*(0.19)*	*130.00*	*(7.00)*	*2.70*	*(0.21)*	*97.11*	*(7.46)*	*32.89*	*(14.55 to 51.04)*	*<0.001~~06~~*
Phone Consultations	*0.57*	*(0.08)*	*12.43*	*(1.78)*	*0.49*	*(0.09)*	*10.69*	*(1.98)*	*1.74*	*(-2.74 to 6.09)*	*0.~~4466~~447*
Home Consultations	*0.06*	*(0.03)*	*7.74*	*(3.24)*	*0.09*	*(0.04)*	*10.39*	*(4.52)*	*-2.65*	*(-11.91 to 5.27)*	*0.~~5528~~553*
Total Consultations	4.24	(0.23)	150.17	(8.90)	3.27	(0.27)	118.19	(10.52)	31.97	(8.38 to 54.22)	0.004~~4~~
Practice Nurse Consultations:											
Surgery Consultations	*1.90*	*(0.18)*	*22.75*	*(2.11)*	*1.41*	*(0.14)*	*16.88*	*(1.71)*	*5.86*	*(1.14 to 11.00)*	*0.01~~5~~6*
Phone Consultations	*0.69*	*(0.09)*	*3.28*	*(0.42)*	*0.15*	*(0.05)*	*0.71*	*(0.25)*	*2.57*	*(1.75 to 3.45)*	*<0.0~~0~~01*
Home Consultations	*0.02*	*(0.01)*	*0.41*	*(0.28)*	*0.01*	*(0.01)*	*0.30*	*(0.27)*	*0.11*	*(-0.38 to 0.77)*	*0.704~~2~~*
Total Consultations	2.61	(0.21)	26.43	(2.27)	1.57	(0.17)	17.89	(1.88)	8.54	(3.46 to 14.15)	0.~~0016~~002
District Nurse Consultations	0.04	(0.02)	0.67	(0.41)	0.15	(0.11)	3.94	(3.05)	-3.26	(-11.94 to 0.39)	0.~~2486~~249
NHS24 Consultations	0.10	(0.03)	4.03	(1.39)	0.05	(0.02)	2.12	(0.79)	1.91	(-0.42 to 4.95)	0.~~1386~~139
LUCS Consultations	0.07	(0.02)	4.34	(1.39)	0.04	(0.02)	2.48	(1.16)	1.86	(-0.89 to 4.83)	0.193~~0~~
Medication			24.07	(2.12)			23.59	(2.20)	0.48	(-5.83 to 6.40)	0.868~~2~~
Accident and Emergency Visits	0.07	(0.02)	6.70	(2.24)	0.10	(0.03)	9.74	(2.98)	-3.04	(-8.87 to 2.47)	0.28~~5~~6
Subtotal Excluding Tele-monitoring			**216.41**	**(11.66)**			**177.95**	**(15.15)**	**38.46**	**(5.59 to 69.87)**	**0.019~~4~~**
Tele-Monitoring Service & Device			70.77						70.77		
Total Healthcare Costs			**287.18**	**(11.66)**			**177.95**	**(15.15)**	**109.23**	**(76.36 to 140.63)**	**<0.000~~0~~1**

* : P-values (two-tailed) for significant difference from zero and Bias corrected confidence interval estimated by non-parametric bootstrap (10,000 replications)

LUCS : Lothian Unscheduled Care Service (out of hours GP or nurse consultations)